Official Journal of the

INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

JUL 21 1949

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VOLUME 6, Number 1

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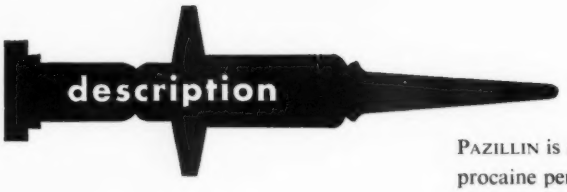

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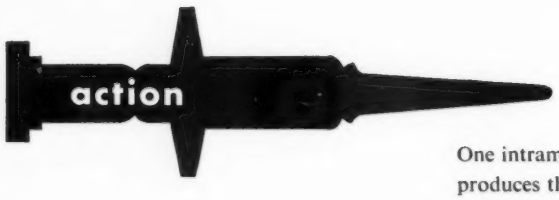

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The Clinical Management of Diarrheas

CHAUNCEY D. LEAKE*

UNIVERSITY OF TEXAS—MEDICAL BRANCH, GALVESTON

OF ALL the intestinal symptoms, diarrhea is the most distressing, accompanied, as it is, usually with pain, nausea, cramp, and colic. It is what people frequently mean when they refer to themselves as having been sick.

Diarrhea is a symptom of prime importance in some conditions like food poisoning, and of secondary significance in others, as in a neurosis. In any situation its relief is welcomed by the patient.

As a symptom, diarrhea is caused by local irritating or inflammatory reactions in the mucosa of the bowel or by intestinal reflexes resulting from autonomic overflow, as in severe emotional states. Self-control of the latter is probably the origin of the phrase referring to having "the guts to take it."

It is amazing how little attention was paid to the therapy of diarrhea by the recent great clinicians. This probably is a reflection of the use of purgation for so many centuries as a routine therapeutic measure. Diarrhea was never taken particularly seriously. Everybody suffered frequently from diarrhea and thought little of it, until recent public health measures became effective.

In our own time physicians have been content often to dismiss the matter as Osler did, with castor oil and tincture of opium. However effective castor oil and tincture of opium may be in general in relieving acute diarrhea, their use is not based upon careful recognition of the facts involved in diarrhea and how it may best be handled in the light of current knowledge.

In handling diarrheas, *specific* management is wisely based upon recognition of the cause. General management, however, may wisely be based upon an appreciation of extent of pathologic physiology produced by the diarrhea in the particular patient under consideration.

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Presented November 12, 1948, before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio.

CAUSES OF DIARRHEA

The causes of diarrhea may be listed as: (1) amebiasis, which perhaps is much more common than ordinarily believed; (2) bacillary infection; (3) "food-poisoning" from bacteriotoxins involving unsanitarily or improperly prepared or preserved food; (4) the important matter of Salmonella infection in infants, or infant diarrhea in general; (5) local irritation from heavy metal or other chemical compounds; (6) allergic reactions, and (7) psychoneurotic reactions.

With regard to amebiasis as a cause it should be remembered that surveys made in various parts of this country show that between 5 and 10 per cent of the people generally harbor the cysts of Endamoeba histolytica. Of this number, some 50 per cent may show symptoms referable to the intestinal tract. Certainly whenever persistent diarrhea is encountered amebae should be carefully sought.

Diarrhea as a secondary symptom is important in many metabolic conditions including: (1) avitaminoses, particularly pellagra and sprue, in which there is a persistent, though sometimes mild, diarrhea; (2) thyrotoxicosis; (3) nephritis, liver cirrhosis, and cardiac decompensation; (4) chronic ulcerative colitis, where we may include many other particular pathologic conditions involving the bowel; and (5) intestinal neoplastic disease. It is always important to remember that diarrhea may be a serious condition in an acute infection.

In the *pathologic physiology of diarrhea,* the most important factor is local irritation, with inflammation and desquamation and with local neuromuscular reflex response involving Auerbach's plexus and the locally contained neuromuscular response. In the presence of local irritation this is sufficient to initiate the peristaltic movement and secretion of fluid into the bowel.

Secretion of fluid into the bowel associated with diarrhea may result in severe dehydration if the diarrhea is acute and intense. Severe dehydration may result in the development of fever and shock. The mechanism of fever production in dehydration, which was first explained by Barbour, is now quite well appreciated.

Associated with the dehydration and loss of water there is always the loss of salt in the bowel, producing a disturbance in electrolyte balance, as Gamble has shown and as Darrow has emphasized, particularly with respect to loss of potassium.

A SERIOUS result of diarrhea may be alteration of intestinal flora. Here it is wise always to remember the delicacy of the balance of intestinal flora, not only with regard to organisms which ordinarily may be present and considered to be nonpathogenic, but also with respect to the balance of various antibiotic factors which normally may be found in the intestinal tract. It is the balance of the organisms in the intestinal tract which is highly important. Under certain conditions, even nonpathogenic organisms may produce reactions and lead to local irritations, and themselves produce diarrhea.

There is the possibility also that nutritional disturbances may occur, from failure of vitamin absorption, from hurried excretion of vitamins, or from failure to take food, in association with nausea accompanying the diarrhea.

CHAUNCEY D. LEAKE

The successful *correction of general pathologic disturbances of diarrheas* depends upon the recognition and appraisal of the extent of the process in the individual patient under consideration. Important factors are the acuity, intensity, and chronicity of the process, and its prolongation, which leads us to the time-intensity relationships in the pathologic physiology of diarrhea.

An acute intense diarrhea is likely to involve a great deal of local irritation and inflammation and result in desquamation of mucosa of the bowel. A prolonged intense diarrhea is likely to involve dehydration and disturbance of electrolyte balance. It is in prolonged mild diarrhea that one is likely to find nutritional disturbances.

The extent of the *water and mineral loss* in diarrhea may be much greater than one might think possible. The average healthy daily intake in an adult is approximately 2,500 cc. of water, made up of about 1,200 cc. of liquids, about 1,000 cc. of water coming in with food or as part of food, about 300 cc. resulting from the water of oxidation in the metabolic process in the body. Ordinarily there is an intake of approximately 4 to 12 gm. daily of sodium chloride. The average healthy daily loss in the feces is only about 100 cc.

of water and about 0.2 gm. of sodium chloride.

In diarrhea, however, varying with the severity, one may lose as much as 500 to 5,000 cc. of water and as much as 2 to 45 gm. of sodium chloride. It is important, then, in considering how to handle the patient with diarrhea, to make a fairly accurate estimate of the extent and severity of loss of water and minerals.

MANAGEMENT OF DIARRHEA

The specific management of diarrheas depends on recognition of the cause. Consider first *amebic infestation*. The diagnosis of amebic infestation can be established only by the specific identification of cysts or motile forms on repeated stool examination. Whenever there is suspicion that amebae may be present or whenever there is an unexplained continuing diarrhea, repeated stool examination is necessary. In any obscure intestinal complaint, repeated stool examination may disclose specific etiologic factors. An important complication of amebic infestation is involvement of other organs, especially the liver.

The dysentery that may be the most important annoying factor or symptom in amebiasis may promptly be controlled by bismuth subcarbonate orally in doses of 4 gm. given every two to four hours until the dysentery subsides. Bismuth subcarbonate, of course, should be employed rather than the subnitrate, to avoid the possibility of the production of nitrous acid in the bowel, with absorption and resulting lowering of the blood pressure. Bismuth subcarbonate is free from the possibility of any breakdown in the bowel or of producing any toxic symptoms. It does not absorb; it coats over the irritated and inflamed areas, and gives relief.

Specific therapy in amebiasis will appropriately involve the arsenical, carbarsone, or iodized hydroxy-quinoline compounds, either vioform or diodoquin. The dosage of these drugs is the same, 0.25 gm. orally twice daily for ten days. If the liver is involved it is necessary to use emetine hydrochloride, as that tends to localize in the liver in higher concentration than in any other part of the body, and thus to give effectiveness in that organ. The dosage for emetine hydrochloride is 1 mg. per kilogram intramuscularly daily for ten days. A total dosage of 10 gm. of emetine hydrochloride should never be exceeded in any patient because of the possibility of cardiac injury.

It is wise in handling amebiasis to avoid arsenicals in liver and kidney involvement, and to beware of emetine injury to heart muscle. It is important to control reinfection when amebiasis is treated. All members of the family, all members of the household, should be carefully examined to find any carrier who may be harboring cysts of the organism without presenting symptoms. Such carriers may be treated effectively with carbarsone. Carbarsone and vioform may readily be administered by retention enema, or vioform may be dusted into the rectal area if there is severe rectal or lower colon involvement. The carbarsone retention enema is highly effective also in the acute conditions.

Associated with amebic infestation may be infestation with Giardia or trichomonads or other intestinal organisms of a similar sort. Few of these are thought to be pathogenic, yet many of them may produce pathogenic symptoms under conditions of disturbance of the ordinary balance involving the intestinal flora.

Consider next the specific management of *diarrheas following bacillary infection*. While the ancient scourge of cholera is almost no more, acute dysentery from the Shiga bacillus and other intestinal invaders may be encountered. The diagnosis is made on the basis of symptomatology and specific identification. The most severe complication results from dehydration following the intensity and acuity of the process. The most effective treatment now available is with phthalylsulfathiazole. The phthalyl derivative of sulfathiazole is insoluble, is not absorbed from the bowel, and is effective in clearing out the organisms even in the presence of a watery dysentery. The dosage is 0.25 gm. per kilogram daily by mouth in 6 equal parts at four-hour intervals.

Precautions to be observed are the necessity of controlling the dehydration, making sure that the water balance is restored, the prevention of reinfection, and the maintaining of water soluble vitamin intake. In convalescence from acute diarrhea it is vital to do everything possible to restore the inflamed, irritated, and desquamated mucosa of the intestinal tract, and this may best be done by high intake of vitamin A, the water soluble vitamins, and particularly the total B complex, and C.

With reference to factors involved in the management of *diarrheas due to food poisoning*, Dack classified food poisoning as due to: (1) irritating chemicals in food which may have been ingested

by accident, as arsenic, zinc, copper, cadmium, or lead; (2) poisonous plants—the oleander, digitalis, aloes, castor and croton bean, and poisonous mushrooms; (3) poisonous animals, in particular poisonous shellfish, poisoning being associated with the absorption of toxic material from plankton at certain times of the year; (4) botulism resulting from unsanitary, ill-prepared food, frequently home preserved; (5) staphylococcal or streptococcal contamination of food with time available for incubation of the organisms and resulting production of chemical toxins which are highly irritating and highly inflammatory; (6) Salmonella infection, and (7) trichinosis.

The diagnosis can best be established by the history and symptomatology with reference to the causes which have been indicated as discussed by Dack. The complications, again, as in the case of bacillary dysentery, are chiefly dehydration or disturbance of salt balance. The treatment that is most effective here is the immediate control of the diarrhea by such an agent as bismuth subcarbonate or powdered opium, 60 mg., followed during convalescence by tea, for the tannin content. It is interesting that most of the folklore remedies for the control of diarrhea are tannin-containing materials, such as barks of various plants.

Precautions involved in the management of food poisoning are, of course, to maintain fluid and water soluble vitamin intake and to control, wherever possible, unsanitary conditions involving food handling.

INFANTILE DIARRHEA

In *Salmonella infection or infant diarrhea* in particular, the diagnosis is established by symptomatology and specific identification. Complications are usually severe in infant diarrhea and are chiefly referable to dehydration and disturbance in ion or electrolyte balance involving particularly the loss of potassium. Fever results from acute dehydration and cardiac and other tissue effects may follow electrolyte loss.

For specific therapy of infantile diarrhea the antibiotic aureomycin is perhaps most promising. This is a new agent. It is active against Salmonella, also against many other types of organisms, including large viruses, rickettsias, and gram-positive and gram-negative bacteria. The dosage is very low, 2 cc. of a 10 per cent solution intramuscularly.

Treatment of infant diarrhea also involves the careful administration of fluid and electrolytes. Here one may particularly consider Darrow's solution, described in his Buchanan Lecture at the University of Texas Medical Branch. This is administered by hypodermoclysis, about 100 cc. per kilogram daily. The solution is in effect 0.44 per cent sodium bicarbonate, 0.27 per cent potassium chloride, and 0.3 per cent sodium chloride, in 5 per cent glucose. Precautions are necessary in the careful administration of potassium-rich solution and in careful control of dehydration and shock.

TOXIC ENTERITIS

In the specific management of toxic enteritis resulting from locally irritating chemical action, the diagnosis is established by history and symptomatology. Complications involve systemic toxicity which may result from absorption, especially involving the liver and kidney with arsenical or mercurial compounds. Treatment here is rather hit or miss and is largely directed toward the precipitation of the chemical in the bowel to prevent further absorption. Precipitation of heavy metals and of alkaloids may be obtained by giving tannin or tannin-containing materials, charcoal, egg white, flour-water, orally and by enema. Precautions include protection of the kidneys by prompt alkalinization. It is wise also to guard generally against heavy metal systemic toxicity by the intramuscular injection of BAL (British antilewisite), di-thio-propanol, 3 mg. per kilogram every four hours, 10 per cent solution in oil and benzyl benzoate. This has been shown to be particularly effective against arsenical and mercurial compounds.

ALLERGIC CONDITIONS

In the specific management of diarrheas due to allergic conditions, the diagnosis is established by history, symptomatology, and differential exclusion. Complications include allergic tendencies in other organs. The treatment may be by benadryl or other antihistaminic compounds. Symptoms may also be relieved by belladonna, 30 mg.; or by atropine, 1 mg.; or by ephedrine, 50 mg. These will produce some degree of relaxation in the bowel.

The most important point is to undertake, if possible, the elimination of the allergic factor, either from the diet or from the environment. Precautions involve the protection of the patient

against ingestion of or contact with the allergic factor. Even if the allergic factor is absorbed from the lungs, the most sensitive tissue may be the bowel and the chief symptom of the allergy may be found in the bowel.

PSYCHONEUROSES

Finally, in the management of diarrheas resulting from psychoneuroses, the diagnosis, again, is established chiefly by history, symptomatology, and differential exclusion. Complications include other symptoms of psychosis or neurosis. It is important to discover, if possible, the trigger stimulus that may initiate the diarrheal or bowel reaction. The treatment here includes chiefly the reconditioning of the individual by psychotherapy. Temporary relief from the diarrhea may be given by the administration of bismuth subcarbonate or belladonna. A factor of precaution here is to beware of a hasty diagnosis. One can readily put the blame for an unexplained diarrhea upon a psychoneurosis when in fact the specific organism that may be present, as in the case of Endamoeba histolytica, has simply not been found.

In summary, it is to be emphasized again that the *specific* management of diarrhea is based essentially upon the recognition of the cause. The general management of diarrhea is wisely based on an appreciation of the extent of the pathologic physiology involved in the symptoms in the individual patient under consideration.

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Intrathoracic Extrapulmonary Tumors

DIAGNOSIS AND SURGICAL TREATMENT

STUART W. HARRINGTON*

MAYO CLINIC, ROCHESTER

MANY different types of tumor occur in the superior, anterior, and posterior mediastinal regions. These lesions may be of congenital embryonic origin, they may arise from tissues normally present in these regions, or they may be acquired lesions, such as result from parasitic disease or trauma to the thorax. Such tumors are often adherent to and impinge on the lungs, heart, and great vessels and may seriously interfere with the function of these organs. In many instances it is difficult to distinguish these tumors from lesions of the great vessels, heart, and lungs.

Increased interest in the diagnosis and treatment of these intrathoracic extrapulmonary tumors has been shown in recent years because they are being encountered more frequently. The incidence of these growths is probably no greater now than it has ever been. One of the important reasons for the more frequent recognition of these tumors in recent years is the use of routine roentgenographic examination of the thorax.

For many years the medical profession has carried out roentgenographic examinations on patients who seek medical attention for some definite complaint but only in recent years has it been done as a routine diagnostic procedure on mass groups of people who have no definite complaint. When an abnormal condition which is indicative of the presence of a tumor is shown in a routine roentgenogram, it is important that complete roentgenologic and physical examinations be made to determine the type of lesion. This should be done regardless of whether or not the condition has caused any subjective symptoms because early diagnosis and immediate institution of treatment are of the utmost importance in managing tumors.

The early diagnosis of these growths before they have made serious inroads on the patient's general condition has been of inestimable aid to their surgical removal and to the final result. Study of proved cases of intrathoracic extrapulmonary tumors has given a different conception than was formerly held of the type of lesion found in the thorax and of the prognosis. The older belief was that most intrathoracic growths were malignant and that only conservative treatment was justified, because surgical treatment was an extremely hazardous procedure. The lack of response of many of these tumors to conservative treatment has encouraged surgical intervention with the view of complete removal of the growth and the marked advancement in methods of surgical technic has made operative removal a relatively safe procedure. Microscopic study of the lesions removed has shown that a large percentage of intrathoracic tumors are benign.

All intrathoracic tumors, however, should be considered potentially malignant. The increased number of benign tumors seen in recent years is

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Presented November 12, 1948, before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio.

due to early recognition and their removal before they have undergone malignant change. Tumors that remain benign often attain enormous size and may cause death from mechanical pressure on the important structures in the thoracic cavity which are adjacent to the tumor. These structures either control, or are closely associated with, respiration, circulation of arterial and venous blood and lymph, deglutition as well as the functional innervation of organs lying outside the thorax. Because of the potential malignant character of these tumors and their close proximity to the important structures contained within the thorax, it is of paramount importance that tumors in this region be recognized early and that treatment be instituted immediately before the growth has become malignant and metastasized or has caused serious and permanent injury from pressure to the vital structures within the thorax.

STUART W. HARRINGTON

DIAGNOSIS

Many difficult problems are associated with the establishment of an accurate clinical diagnosis as well as the selection of the most effective method of treatment for these growths. These problems are best solved by the close cooperation of the clinician, roentgenologist, and surgeon.

The clinical manifestations of benign intrathoracic tumors are often meager and rarely pathognomonic, although they are always of great value when correlated with the roentgenologic findings in the establishment of a final diagnosis and in the selection of the type of treatment to be instituted. Even after correlation of the results obtained by application of all of the modern thoracic diagnostic methods, it is often impossible to determine clinically the type of lesion that is present or whether the tumor is benign or malignant.

From a study of the type of tumor in proved cases it has been found that the position of the tumor in the thoracic cavity is of great value in suggesting the type of tumor present, for certain types of growth are more likely to occur in certain locations than in other locations. In a general way, it may be stated that the most common type of tumor in the anterior mediastinum is the teratoid growth but this type of tumor is found occasionally in the posterior mediastinum also (Figures 1 to 4). Other tumors which are found often in the anterior mediastinum are thymic tumors and cystic tumors.

The most common tumors located in the posterior mediastinum are perineural fibroblastomas or neurofibromas, although these tumors also may be located along the course of the nerves along the lateral wall of the chest as well as in the spinal column. The more common lesions in the middle mediastinum are the lymphoblastomas and aneurysms which usually are not treated surgically. Lesions in this location require the greatest care in differentiation from a surgical standpoint because in this region lesions not susceptible to surgical treatment are most likely to be present.

Tumors of the superior mediastinum also present difficulty in differentiation because they fill the entire space so that it is difficult to evaluate the surrounding visceral relationship. The most common tumors located in this region are thymoma, intrathoracic goiter, neuroblastomas, aneurysm, cystic lymphangioma, as well as cysts of the lung, particularly the cystic azygos lobe.

Tumors situated in the anterior mediastinum as a rule cause more subjective symptoms than those situated in the posterior mediastinum, because of the smaller space in which they are confined. This is true whether the lesion is benign or malignant.

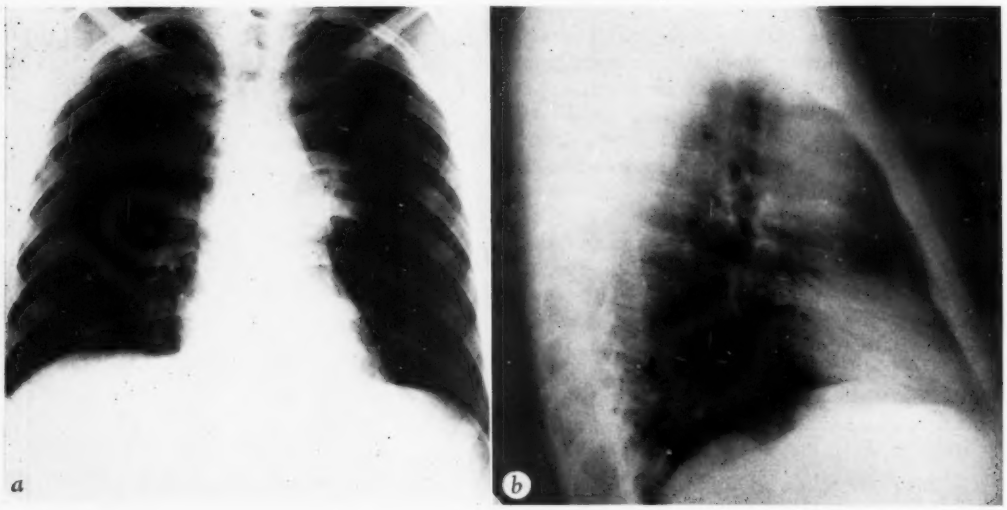

Figure 1. Anterior mediastinal teratoma containing adenocarcinoma, grade 3, of a man, aged 38 years which produced no symptoms. Tumor found on routine roentgenologic examination. *a* and *b*. Rounded tumor in left superior anterior mediastinum at level of arch of aorta.

Pain is one of the most important subjective symptoms of these growths. Anterior mediastinal tumors usually are accompanied by pain, whether they are benign or malignant, but the pain of benign tumors is never as severe as that associated with malignant lesions.

When lesions are benign, the patients have a sense of pressure beneath the sternum, usually associated with dyspnea on physical effort. These symptoms are progressive in character, and are associated with, and augmented by, inflammatory lesions of the respiratory tract. These tumors are commonly diagnosed as pulmonary or pleural lesions, such as pleurisy, pneumonia, or influenza. When anterior mediastinal tumors become malignant, the pain is usually more severe; at first it occurs periodically and is noted mostly at night. It gradually becomes more or less constant until sedatives are required for relief.

Posterior mediastinal tumors may be benign or malignant (Figures 5 to 8). Benign tumors in this location are the most silent tumors that occur within the thorax. The outstanding clinical features are relatively few and only mild symptoms may be associated with large growths, for these tumors may fill practically the entire hemithorax without producing any marked symptoms other than dyspnea on exertion. When tumors situated in this region are malignant, or have undergone malignant change, relatively small growths are associated with severe pain; the patient's chief complaint is of the pain.

Dyspnea and other clinical manifestations are usually more marked when the tumor is situated in the upper part of the posterior mediastinum, because in this region the growth not only produces pressure on the lung itself, but in many instances it causes direct pressure on the large bronchi and on the hilus of the lung; at times, also, it exerts pressure on the trachea and thus causes marked interference with respiration, particularly on exertion. With this latter condition there is often associated compression of the esophagus that causes some difficulty in swallowing.

Bronchoscopic and esophagoscopic examinations often are aids in establishment of the diagnosis by disclosing the presence of an extrinsic tumor which causes pressure on the bronchus or esophagus. These examinations are rarely conclusive. Thoracoscopic examination, after induction

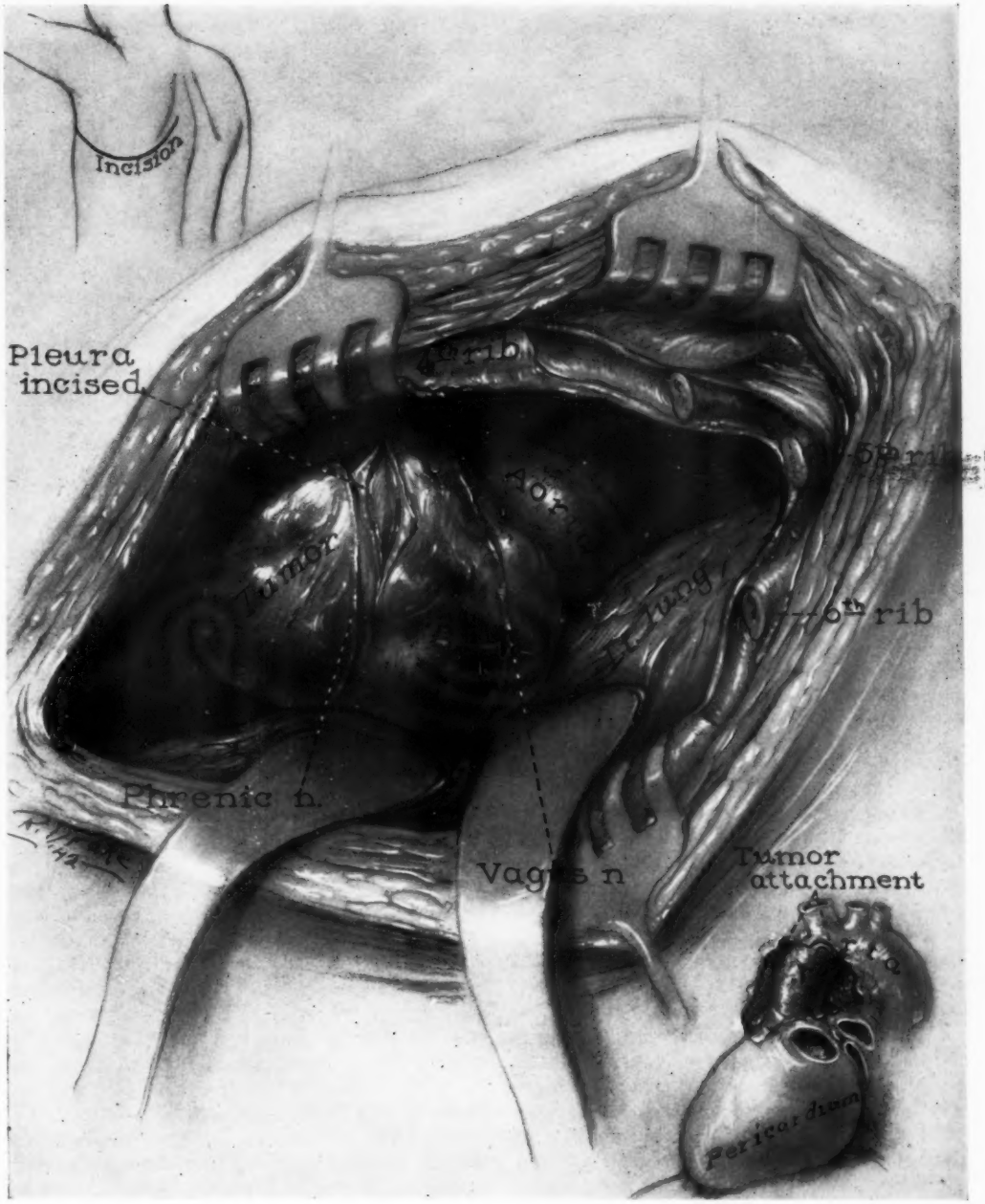

Figure 2 (same case as in Figure 1). At operation; rounded mediastinal tumor adherent to aorta and upper part of pericardium. Complete left posterolateral transpleural removal of teratoma.

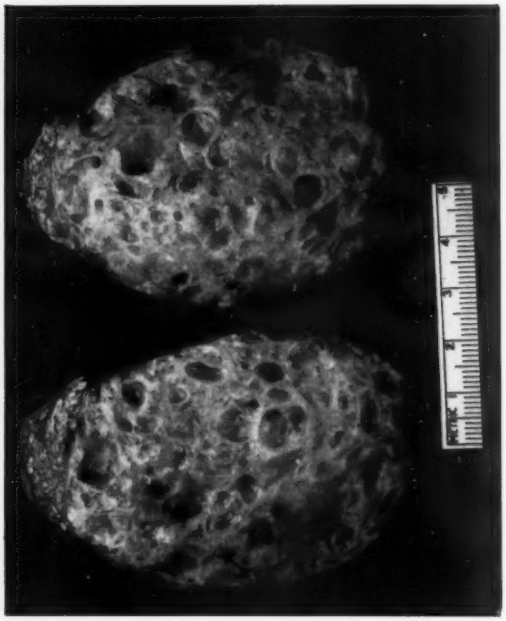

Figure 3 (same case as in Figures 1 and 2). Cystic teratoma containing squamous epithelium, various types of glands, fat, smooth muscle, cartilage, pancreas, thymic tissue, nerve tissue, glial tissue and hair and small regions of adenocarcinoma, grade 3.

of artificial pneumothorax, may be of value, and a definite diagnosis often can be made by removal of a portion of the tumor through the thoracoscope. In most instances, however, sufficient information can be obtained from the more conservative methods of diagnosis to determine the advisability of surgical intervention; in such cases I prefer to perform exploratory thoracotomy.

Roentgenologic study—The most important of the clinical aids to diagnosis is the roentgenologic study. For this roentgenograms taken in different positions as well as roentgenoscopic examination of the thorax are required. The single roentgenogram is of little value in the surgical consideration of these tumors, for it indicates only the presence of the tumor and its position in one plane of the thorax. Anteroposterior and lateral stereoroentgenograms are of great aid in determining not only the situation of the tumor in the thorax, but also the relation of surrounding normal structures to the tumor and any encroachment that the tumor has made on these structures. Anteroposterior stereoroentgenograms indicate especially accurately the situation of the tumor in the vertical plane of the thorax, and the lateral views indicate especially accurately the relation of the tumor to the anterior and posterior thoracic walls.

Roentgenoscopic examination does not furnish as much detail as stereoroentgenograms do, but is of great value in the determination of the normal functional activity of intrathoracic structures, and any impairment of these structures which may have been caused by the tumor. It also is especially important in the differential diagnosis of aneurysm from anterior mediastinal tumor. Here the differential diagnosis is often made difficult by the adherence of dermoid cysts and teratoid tumors to the pericardium and great vessels, which causes transmitted pulsations. Horizontal roentgenograms are of value in selected cases; they are taken in different positions to determine fluid level within the pleural cavity or within the walls of a cystic tumor.

In many cases the diagnosis is still obscure even after roentgenoscopic examination and the taking of an entire series of roentgenograms in different positions. In some of these cases, additional information can be obtained by taking another series of roentgenograms after production of artificial pneumothorax, or after introduction of barium into the esophagus, and, in some instances, of iodized oil into the bronchial tree.

Roentgen therapy is often of great aid in the differential diagnosis of radiosensitive tumors. This is of particular importance in the selection of cases for surgical intervention, for one of the most important lesions to rule out is mediastinal lymphoblastoma. These growths are not amenable to surgical treatment, and in the roentgenograms they can simulate the appearance of practically any other primary intrathoracic growth. A definite diagnosis of lymphoblastoma often can be made by complete roentgenologic study.

In cases in which there is any doubt, roentgen therapy should be utilized, for these tumors are radiosensitive and will rapidly diminish in size, and practically disappear, in a relatively short time. Some diminution in the size of the roentgenologic shadow of the growth can be noted as early as five to seven days after the initial treat-

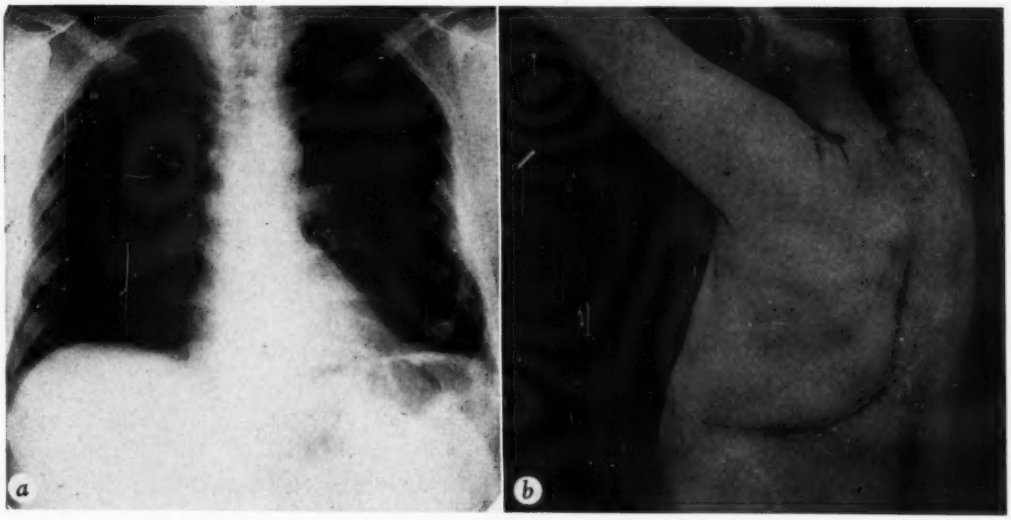

Figure 4 (same case as in Figures 1, 2, and 3). Two years after complete transpleural removal of tumor. *a.* No recurrence of tumor. Lung fields are normal. *b.* Posterolateral incision entirely healed. No subjective symptoms.

ment. It is important that the same technical methods, particularly as to the distance of the patient from the film, be used for patients who are being kept under observation or treatment, so that any change in the size of the roentgenologic shadows will be caused by variation in the size of the lesion and not by variation in technic.

Roentgenologic studies of the thorax are of great importance in those cases of mediastinal tumors in which surgical treatment is considered. Not only do they assist in selection of operable growths, but also they aid in determining the most accessible type of approach to the tumor and in determining the presence of conditions that might, after operation, become complications.

SURGICAL TREATMENT

The most important considerations in the surgical treatment of mediastinal growths are early diagnosis, preoperative preparation of the patient, selection of the most accessible method of approach, application of adequate mechanical means for maintaining intrapulmonary pressure, complete removal, and postoperative care of the patient. The significance of early diagnosis of malignant growths is obvious. With benign growths it is important to institute surgical treatment before the tumor has encroached on important structures within the thorax, or before it has attained such great size that the operative risk is very greatly increased.

Much of the advancement that has been made in surgical removal of intrathoracic growths has been accomplished because of marked improvement in the administration of anesthetic agents. The greatest immediate danger in intrapleural operation is collapse of the lung from open pneumothorax. This may produce severe respiratory and circulatory disturbances which may result in sudden death. This danger has been practically eliminated by the use of intratracheal anesthesia, induced by means of an apparatus by which gas and oxygen are given under positive pressure.

Administration of the anesthetic agents should be in the hands of a skilled anesthetist. In cases in which partial collapse of the lung is required, the lung should be permitted to expand fully every ten to fifteen minutes during the course of the operation. A suction pump should be applied to the intratracheal catheter before it is withdrawn, to remove any mucus that may have accumulated in

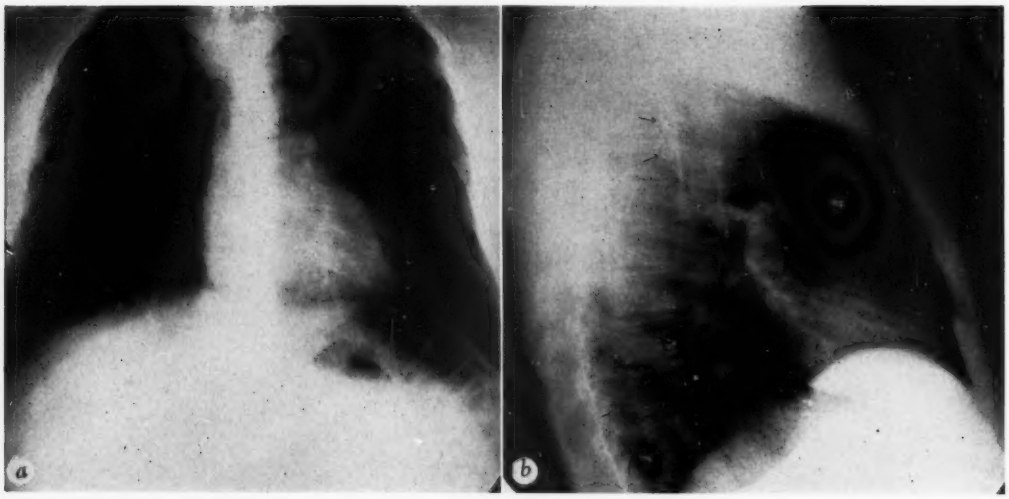

Figure 5. Bronchogenic cyst of right upper part of the posterior mediastinum adherent to the trachea of a man, aged 34 years who had no subjective symptoms. Tumor was found on routine roentgenologic examination of the thorax. *a* and *b*. Circumscribed tumor of right upper part of mediastinum posterior to the trachea. Roentgenoscopic examination revealed that tumor moved with swallowing. Condition previously diagnosed as intrathoracic goiter.

the trachea. It may be stated that use of intratracheal positive pressure anesthesia has been of the same relative importance to the technical problems associated with surgical removal of these growths as roentgen rays have been to the clinical diagnosis of the lesions.

THE more important technical considerations associated with surgical removal of these growths are as follows: (1) Access is through the bony encasement of the thorax, and a method of approach must be selected that will give the greatest exposure of the tumor with the minimal amount of trauma to the thoracic viscera and thoracic wall; (2) traction on the important structures in the mediastinum, to which the tumor might be adherent, is an element of danger; and (3) complete reconstruction of the thoracic cage, in order to restore the normal relations of the thoracic viscera and to give the minimal amount of deformity, is advisable.

The methods of approach to, and the types of operative procedures for, mediastinal growths depend on the site of the tumor, its extension within the thoracic cage and the presence of complications which may have been produced by the growth. In each case the approach must be selected individually, on the basis of the indications presented. A few general principles apply to all cases. The most important is early operation and complete removal of the tumor; this may be performed in multiple stages but I prefer to remove the growth in one stage if possible, for the second operation may be more hazardous and difficult than the first. Incomplete removal of the growth may be followed by more serious trouble and usually a subsequent operative procedure will be required.

Anterior mediastinal tumors may be approached through the anterior or posterior wall of the thorax, but I prefer the posterior approach, particularly when the tumor projects into either pleural cavity (Figures 9 to 13). It gives much greater exposure than the anterior approach and it permits dissection under direct vision of the tumor from the important structures to which it may be adherent. These usually are the heart, the great vessels, and the lungs. Furthermore any injury to these structures caused by the tumor or operative

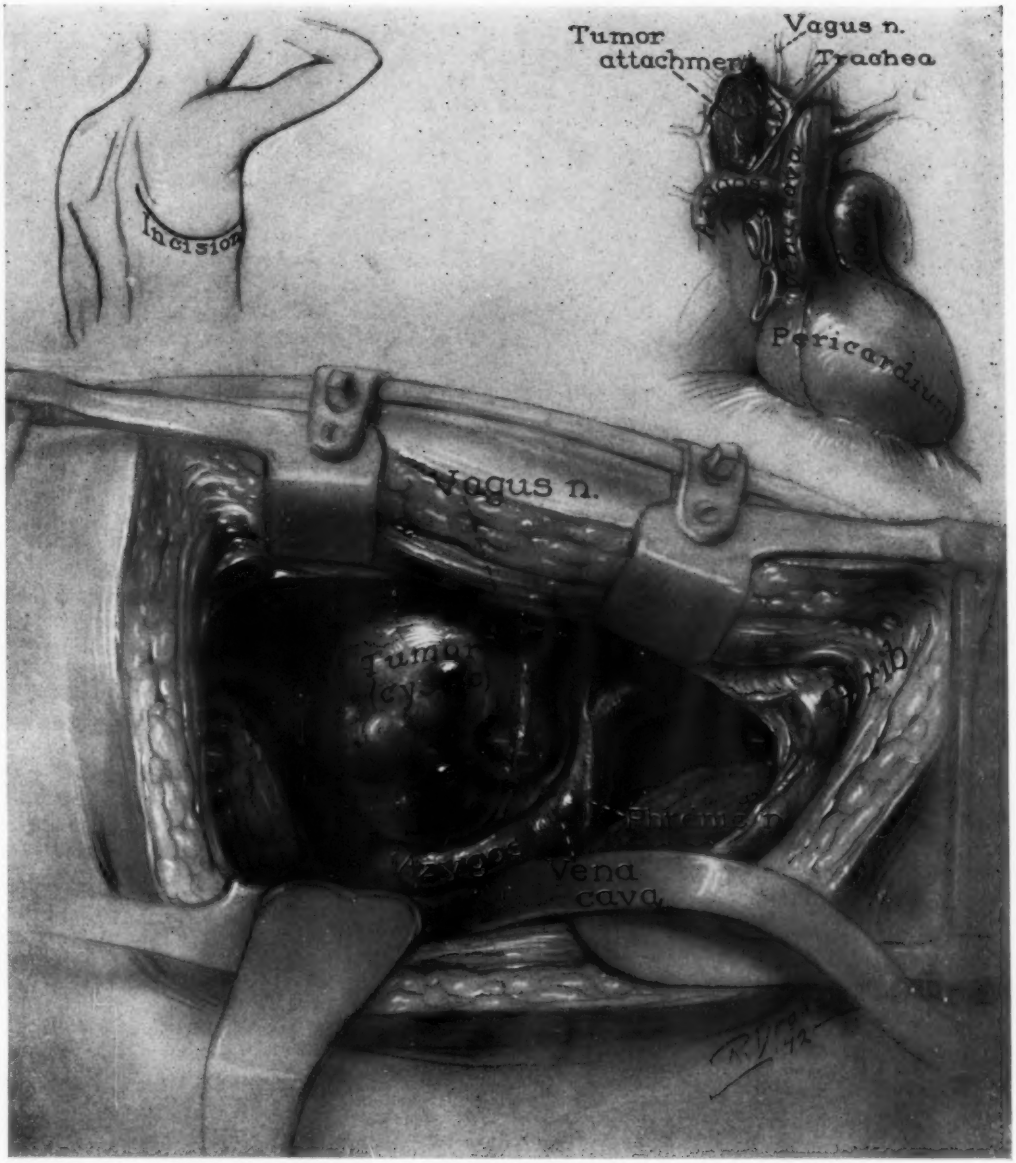

Figure 6 (same case as in Figure 5). At operation; right posterior transpleural complete removal of bronchogenic cyst located in the posterior superior mediastinum above the azygos vein, and firmly adherent to trachea.

procedure can be detected and repaired immediately, and if infection is encountered, drainage can be instituted readily.

If the tumor is small and is confined to the anterior or superior mediastinum, or if it has ruptured into the lung anteriorly, the growth may be

Figure 7. Gross specimen of bronchogenic cyst containing mucoid material and lined by stratified ciliated epithelium, with smooth muscle and areas of calcareous degeneration in the walls.

more accessible through an interior approach. This may be achieved by splitting the sternum or removing the cartilage and turning back the wall of the thorax. In many instances such tumors can be removed extrapleurally through an anterior type of incision, while the operation is transpleural when the posterior approach is used.

The approach to posterior mediastinal tumors is practically always through the posterior thoracic wall, and an attempt always should be made to remove the tumor extrapleurally. This, however, rarely can be accomplished and only in cases in which growths are small, for the tumor usually is adherent to the parietal pleura, which is ultimately opened; in some instances the tumor is placed so far back in the mediastinum that it is impossible to dissect the pleura away from the thoracic wall sufficiently to permit the removal of the tumor.

Tumors situated in both the posterior mediastinum and spinal cord, often called "dumbbell" or "hourglass" tumors, are removed by posterior mediastinotomy and laminectomy (Figures 14 to 17). This may be done in one or two stages. If the tumor is removed in two stages, the intraspinal portion of the tumor should be removed first by

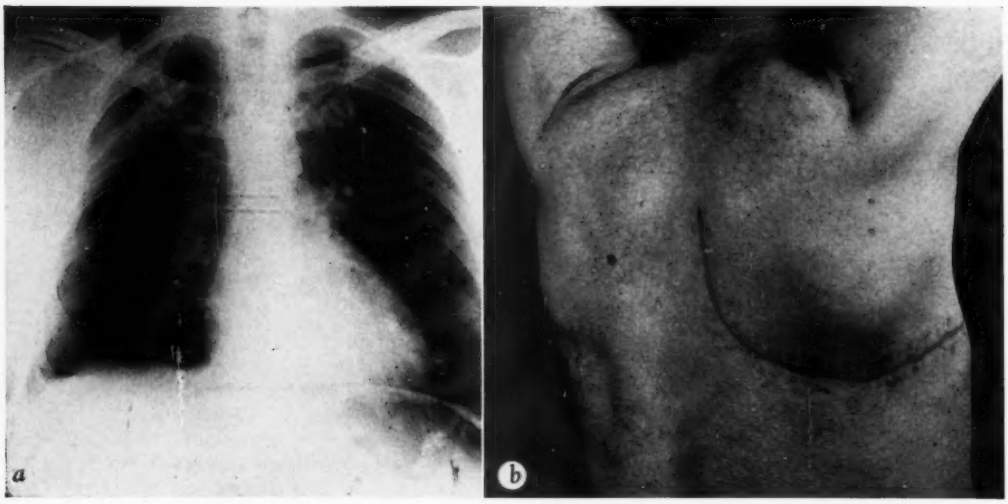

Figure 8 (same case as in Figures 5 and 6). Two years after posterior transpleural complete removal of bronchogenic cyst. *a.* Lung fields give no evidence of disease. Thickened pleura in right base. *b.* Wound healed and the patient had subjective symptoms.

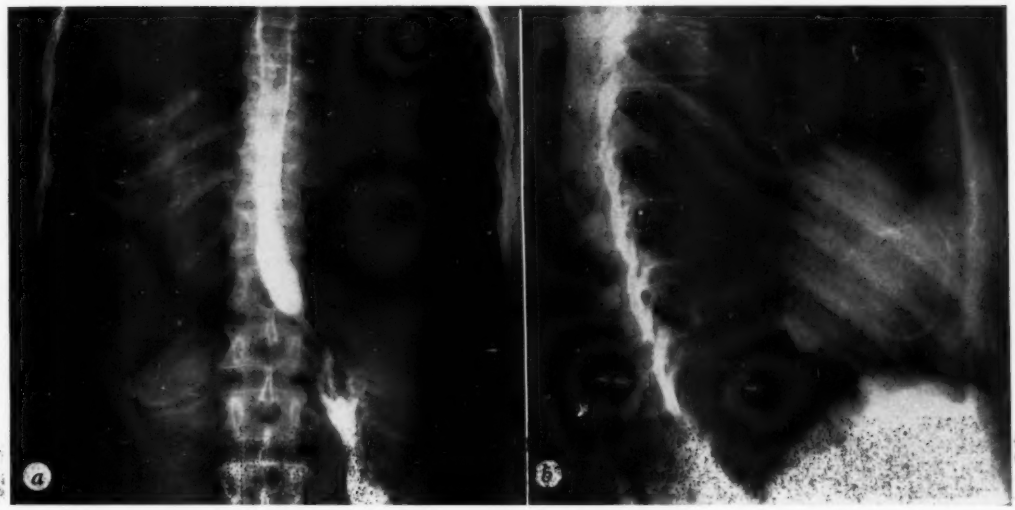

Figure 9. Large cystic calcareous thymoma of anterior mediastinum, extending into right side of the thoracic cavity. Patient was a woman, aged 42 years, who had had dyspnea, convulsions, and weakness. She had lost 25 pounds (11.3 kg.) in one year. *a* and *b*. Large tumor (thymoma) of the right anterior portion of the mediastinum in front of heart shadow and extending to, and adherent to, diaphragm. Esophagus normal.

laminectomy to minimize the danger of permanent damage to the spinal cord from pressure caused by edema of the tumor or hemorrhage into the spinal canal. The mediastinal portion of the tumor usually can be removed by posterior mediastinotomy ten to fourteen days later. The two-stage procedure is usually indicated when the mediastinal portion of the tumor is large because collapse of a large amount of lung and other intrapleural complications may greatly increase the operative risk.

When the mediastinal portion of the tumor is small, the two procedures may be done at one time through two separate incisions. The laminectomy is done first to expose the intraspinal portion of the tumor and then a posterior mediastinotomy is done with complete removal of both portions of the tumor through the mediastinum. This one-stage procedure is preferable in selected cases because it avoids any possibility of leaving a portion of the tumor, hemostasis can be more accurate, and in some cases the mediastinal portion of the tumor can be removed extrapleurally.

The situation of the incision in the thoracic cavity depends on the location of the tumor. In all cases in which the tumor is situated in the posterior mediastinum, a posterolateral incision is made around the vertebral border of the scapula. The entrance into the thoracic cavity is made by partial resection of one rib, over the most central portion of the tumor. The thoracic cavity is then opened by incising through the periosteum and pleura in the bed of the rib. The tumor and its attachments in the pleural cavity are then explored, and if further exposure is desired, it can be accomplished by partial resection of an adjacent rib. In some cases in which there is a small tumor, or a collapsible cystic tumor, the growth may be removed through this small opening. If a larger opening is required, for a large solid tumor, the bordering ribs, both above and below the resected rib, are cut and drilled, and at completion of the operation the cut ends are sutured together to reestablish the contour of the thoracic wall. Extreme care should be taken not to injure the structures within the thorax to which the tumor is adherent. There is usually a fairly definite covering over the tumor, which consists of pleura and the capsule of the tumor. This capsule often contains many large vessels if the tumor is large.

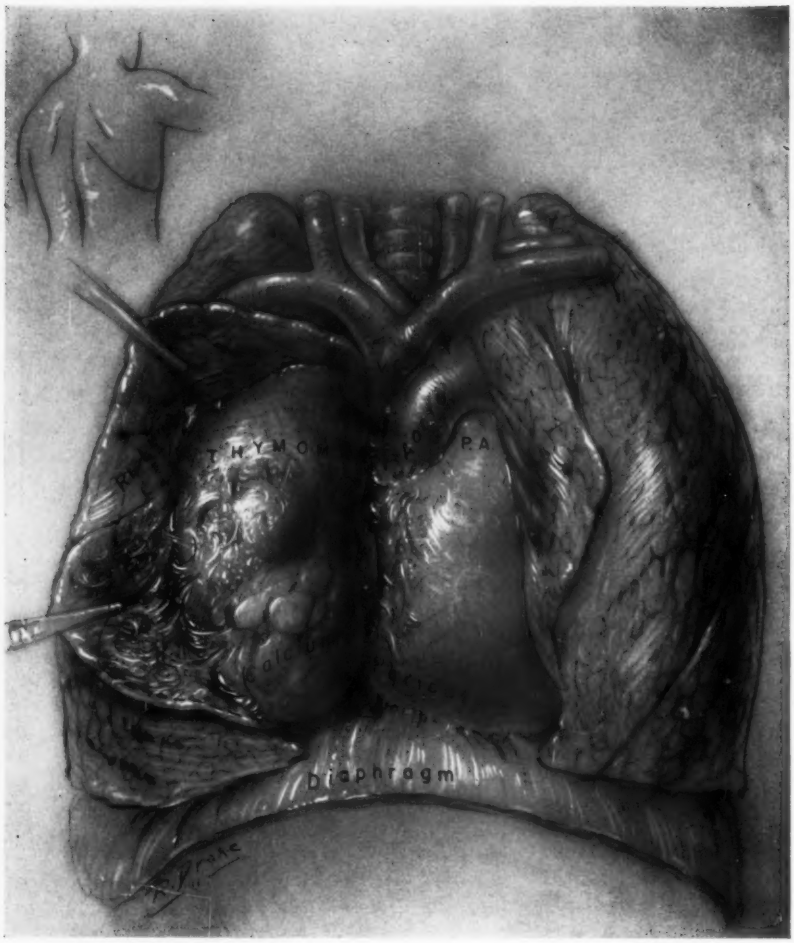

Figure 10 (same case as in Figure 9). At operation: complete, right posterolateral transpleural removal of anterior mediastinal thymoma firmly adherent to the mediastinal surface of the right lung and pericardium and extending to the diaphragm.

By careful dissection, this capsule usually can be separated from the adherent lung without any great injury to the lung. In some of the cases in which large tumors are adherent to the lung, it is necessary to dissect the lung away from the tumor. Careful hemostasis, involving attention to the vessels on the surface of the lung, then is required. Posteriorly these tumors are often very adherent around the aorta, particularly on the left side, and great care should be exercised not to injure the wall of the aorta. Also, care must be exercised to ligate the intercostal vessels that may be severed in the course of removal of the tumor. The greatest difficulty in hemostasis is often encountered posteriorly from the intercostal vessels. In some cases, in which some erosion of an intervertebral foramen has taken place, hemorrhage may occur from dilated vessels in the spinal cord.

After complete hemostasis has been obtained, as much as possible of the raw surface produced by the removal of the tumor from the mediastinum or chest wall, is covered with pleura. The pleural cavity is irrigated with physiologic salt solution to remove any particles of tissue or blood clot, the

Figure 11 (same case as in Figures 9 and 10). Large cystic calcareous thymoma weighing 462 grams.

lung is fully inflated by increasing the positive pressure, and 240,000 units of penicillin is placed in the pleural cavity. The incision is then closed. The pleural cavity is drained by air tight or closed type of drainage with a 22 F. catheter and application of gentle suction to the catheter.

Institution of closed drainage is usually through the posterior periosteum of the rib which has been resected or if this is not an adequate position for drainage of the pleural cavity, a closed type of intercostal drainage is instituted through the eighth interspace posteriorly. This permits drainage of the bloody serum which usually occurs after removal of these growths or when there is trauma to the pleura. The immediate drainage of this bloody serum permits rapid and complete re-expansion of the lung and rarely continues for more than forty-eight to seventy-two hours at which time the drainage tube is removed.

POSTOPERATIVE CARE

The postoperative care of these patients is important and may be divided into two periods.

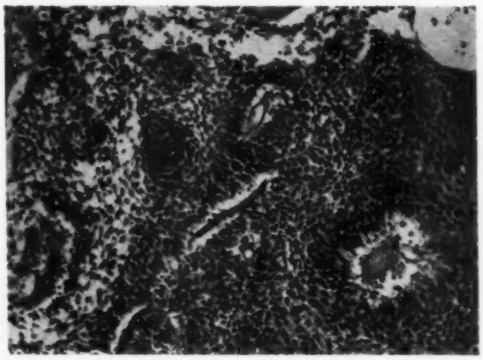

Figure 12 (same case as in Figures 9 to 11). Cystic calcareous thymoma.

First, the immediate postoperative care in the operating room and second, the subsequent postoperative care after the patient returns to his room. The immediate postoperative care begins at the time of operation and consists of the supportive measures needed to maintain the blood pressure and relieve any respiratory difficulty during the operation. It is usually advisable to give some type of medication during the operation or afterwards. If there is much loss of blood during the operation, a transfusion should be given.

Respiratory difficulty is the most serious immediate complication after operation and should be entirely relieved before the patient is permitted to leave the operating room. The trachea and bronchi should be aspirated through the intratracheal tube before it is removed. If there is excessive mucus, the patient should have a bronchoscopic aspiration before being taken from the operating room. Roentgenograms of the thorax and upper abdomen should be taken while the patient is still on the operating table, developed immediately and read before the patient is permitted to leave the operating room. If roentgenograms of the thorax show pulmonary congestion or collapse of the lung, immediate measures should be taken to correct the condition and further roentgenograms should be taken and again read before the patient is returned to his hospital room.

It is most essential not to remove the patient from the operating room until the bronchi are entirely clear of mucus and on some occasions it may be advisable to keep the patient in the operating room until he has fully recovered from the

Figure 13 (same case as in Figures 9 to 12). Nine months after transpleural removal of thymoma. *a*. Mediastinum and lung fields are normal. *b*. Wound had healed. Patient had no subjective symptoms and had gained 32 pounds (14.5 kg.).

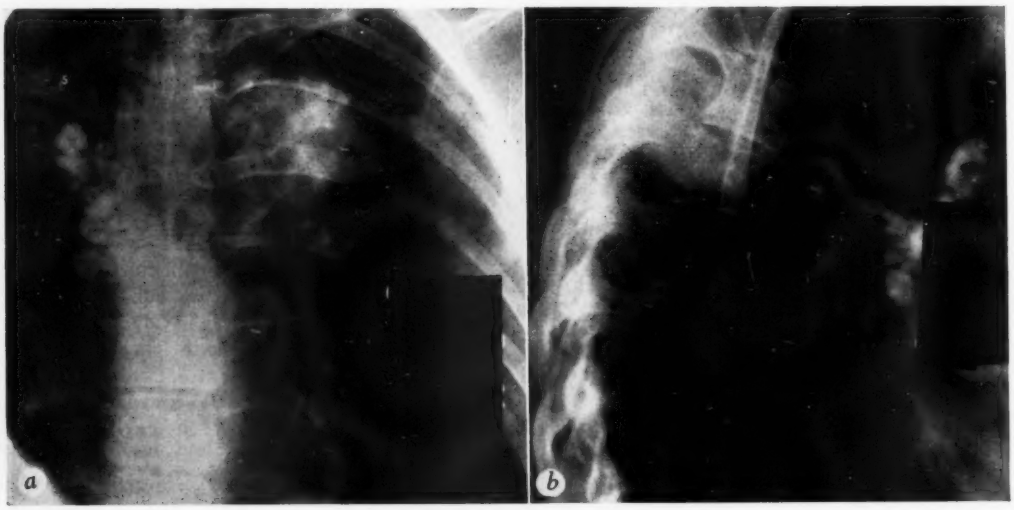

Figure 14. Posterior mediastinal and intraspinal neurofibroma (dumbbell tumor) in a woman, aged 34 years. Numbness and weakness of legs. *a* and *b*. On admission; left posterior mediastinal tumor causing pressure erosion of fifth and sixth ribs posteriorly and enlargement of intervertebral foramen.

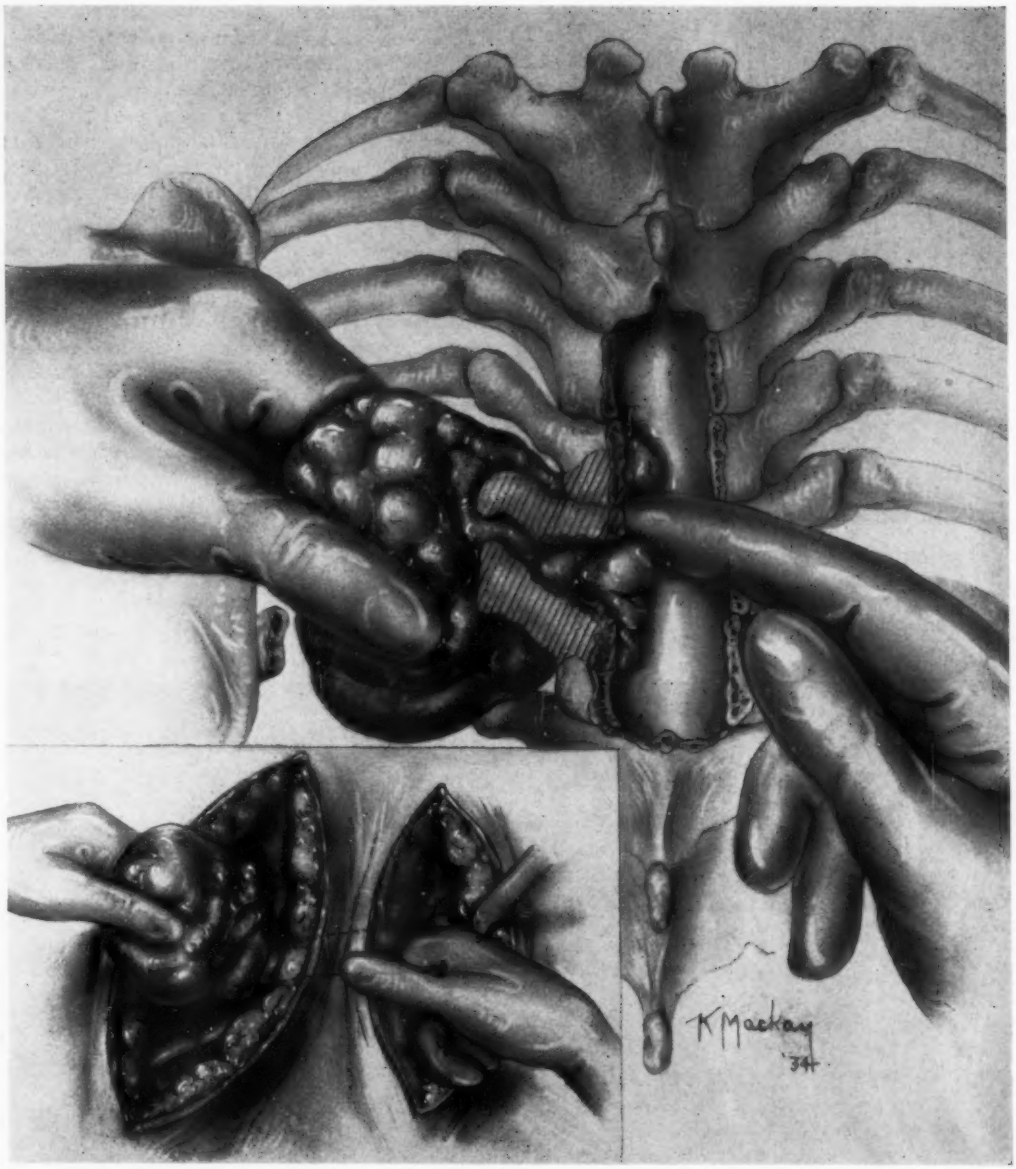

Figure 15 (same case as in Figure 14). *a.* At operation; technic of posterior extrapleural one-stage mediastinotomy and laminectomy for complete removal of (dumbbell) neurofibroma. (From HARRINGTON, S. W., and CRAIG, W. McK.: Mediastinal and intraspinal perineural fibroblastoma [hourglass or dumbbell tumor] removed by one-stage operation. J.A.M.A. 103:1702-1704 [Dec. 1] 1934. By permission of the publisher.)

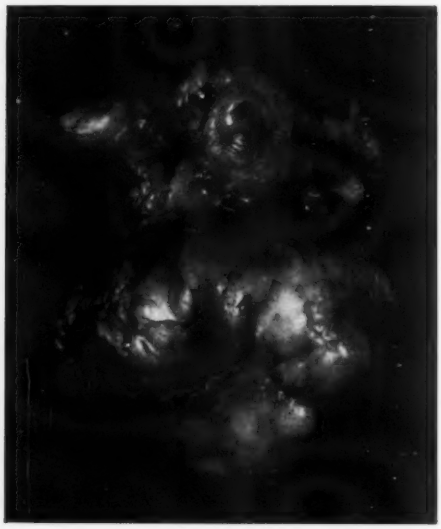

Figure 16 (same case as in Figures 14 and 15). Mediastinal and intraspinal neurofibroma.

anesthesia and the cough reflex is established. This is rarely necessary but in some cases in which the lung has been more or less collapsed by the tumor for a long time, it does not re-expand readily after removal of the growth.

In many cases much of the pulmonary congestion can be minimized by not permitting the lung to be collapsed more than ten to fifteen minutes at one time during the removal of the tumor. After being collapsed for this period of time, the lung should be fully re-expanded for three or four minutes to re-establish aeration and circulation of the blood before it is permitted to collapse again for continuation of the removal of the tumor.

If the roentgenograms of the upper abdomen show dilatation of the stomach with gas, which not infrequently occurs following positive pressure anesthesia, this should be relieved immediately by the use of an indwelling stomach tube which is placed on suction. This tube may be removed after the accumulated gas has been removed or it may be left for a few days during the patient's immediate convalescence to remove any gastric secretions and to

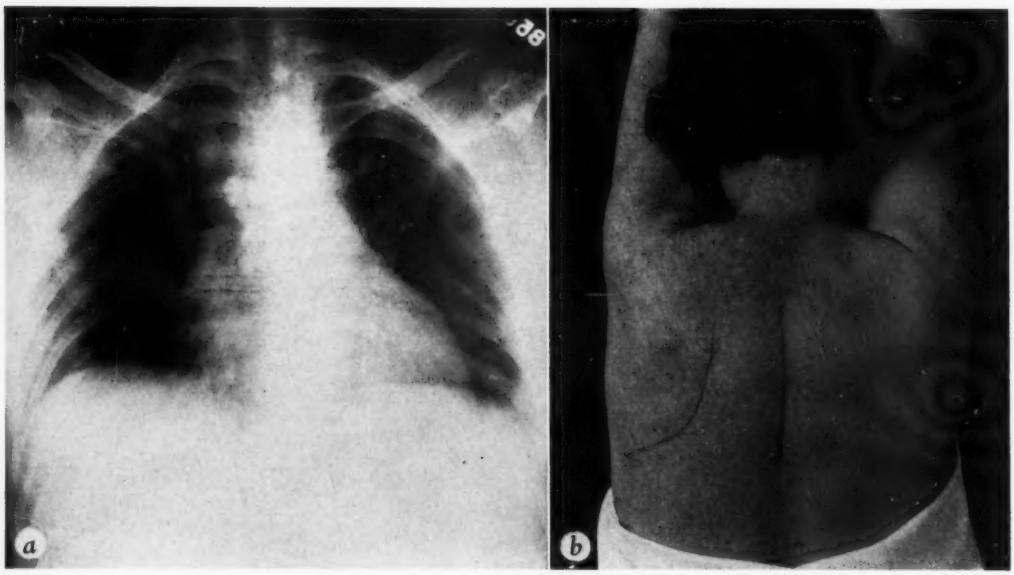

Figure 17 (same case as in Figures 14 to 16). Two years after operation. The patient had no symptoms. *a.* Pulmonary fields normal. Metal hemostasis clips may be seen around spinal column. *b.* Mediastinotomy and laminectomy wounds healed.

prevent vomiting. If this gas is permitted to remain in the stomach, it may cause acute dilatation.

When the patient is taken from the operating room, he is placed in an oxygen tent in which the concentration of oxygen is maintained at 50 to 55 per cent. The tube in the pleural space is placed under gentle suction or under water for closed drainage. The patient is kept in oxygen for varying periods; the duration depends on whether or not respiratory difficulty occurs. However, after removal of the extrapulmonary lesions, oxygen is rarely necessary for more than twenty-four hours. The subsequent postoperative care consists of reestablishing normal respiration and circulation and depends on the progress.

SERIES STUDIED

My experience in the surgical treatment of intrathoracic extrapulmonary tumors consists of a series of 168 cases. The classification of the 168 tumors of this series based on a histopathologic study of the lesions, is as follows: Fifty-one (30.3 per cent) were classified as neuroblastomas. Of these 51 neuroblastomas, 44 were neurofibromas, 4 were gangliomas, and 3 were sympathico neurofibromas. Forty-seven were situated in the posterior mediastinum; 6 of these 47 were both posterior mediastinal and intraspinal tumors, so-called dumbbell or hourglass type of neurofibromas. Three of the 51 neuroblastomas were in the anterior mediastinum and 1 was situated in the lateral wall of the chest. Three (5.9 per cent) of these 51 primary nerve tumors were malignant.

Eleven (6.5 per cent) of the entire series were classified as various types of fibromas. Six (55 per cent) of this group were found to be malignant and were designated as sarcomatous types of malignancy. This is an unusually high percentage of malignant lesions for this group and it is probable that some of these lesions originated as neurofibromas. Roentgenologic findings and location of these tumors in the posterior mediastinum indicated the probable diagnosis of neurofibroma clinically. The subjective symptom of pain associated with some of these tumors indicated a malignant tumor clinically.

Forty (23.8 per cent) of the entire series were classified as different types of teratoid tumors. Thirteen were of the dermoid type of teratoma in which the predominating tissue was ectoderm. In these cases the epidermis lined the tumor and the teratoma in one was of such high degree of organization that it was termed a "fetal parasite." This tumor was covered with epidermis.

Six (15 per cent) of these teratoid tumors had undergone malignant change.

There were eight thymomas (4.7 per cent) of the total series; 7 of these were in the anterior part of the superior mediastinum and one was on the lateral wall of the chest.

There were 5 intrathoracic adenomatous thyroids (3.0 per cent) of the series, all of which were below the third rib anteriorly and 1 extended to the diaphragm.

Thirty-six (21.4 per cent) of the tumors were classified as cysts of the mediastinum. Of these 7 were celomic or pericardial cysts; 8 were endothelial cysts; 3 were cystic lymphangiomas; 10 were bronchogenic cysts; 4 were enterocystomas of the esophagus; and 4 were cysts of the azygos lobe of the right lung. None of these tumors were malignant. This group of 36 does not include the benign tumors of the wall of the esophagus which may simulate posterior mediastinal tumors.

There were 5 endotheliomas and 5 hemangioendotheliomas; 3 tuberculomas in the posterior mediastinum; 1 hamartoma in the anterior mediastinum; 1 lipoma in the anterior mediastinum; and 2 organized calcareous hematomas.

In the total of 168 cases, the tumors were completely removed by transcostal intrapleural or extrapleural operation and in the 6 cases of posterior mediastinal and intraspinal neuroblastomas of the dumbbell type, laminectomy and mediastinotomy were performed.

There were 7 operative deaths (4.2 per cent) in the total series. Three of the patients who died had neuroblastomas; 1 of these had a tumor of the dumbbell type for which laminectomy and mediastinotomy were required. Two of the 7 patients had teratoid tumors, of which 1 was benign and 1 had undergone malignant change. One patient had a thymoma and 1 patient a hemangioendothelioma.

One hundred sixty-one patients recovered from operation. In these 161 cases 33 tumors were malignant. Subsequent examinations to the present time have shown that approximately 50 per cent of these patients had recurrence of the lesion and have subsequently died from malignant disease. The results in the 128 benign lesions were very satisfactory. All patients have been relieved of symptoms and there has been no recurrence of the tumor.

Modern Treatment of Syphilis

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To those who have had limited experience with the many current regimens for the treatment of syphilis, a difficulty is sometimes presented in deciding which should be the recommended form of therapy. Therefore, I thought a discussion of some of the acceptable plans for the treatment of early syphilis, syphilis in pregnancy, or central nervous system syphilis would be of value.

Mahoney[1] first recommended penicillin in the treatment of syphilis in 1943. He must have had spiritual guidance in choosing a dosage schedule of 20,000 units every three hours for 60 doses. While this surpassed any previous form of syphilis therapy, the Syphilis Study Section of the National Research Council thought that the percentage of cures might yet be increased, and so organized several clinics in which other penicillin schedules for the treatment of syphilis were introduced and studied.

One can see, from a compilation of data derived from these studies, that many schedules were tried. For instance, a schedule consisting of only 64,000 units of penicillin as a total dose was used; Figure 1 shows that with this small amount of penicillin the failure rate was around 60 to 65 per cent over a period of approximately nine months. Other schedules using amounts of penicillin from 64,000 to 300,000 units also had a high failure rate; with amounts of penicillin varying from 300,000 to 600,000 units the failure rate decreased but was still high. Other schedules of 1,000,000 to 1,200,000 units of penicillin and 2,000,000 to 2,400,000 units of penicillin were used. In comparing these latter two schedules the difference between these curves is relatively insignificant, and therefore, one can say that the minimal effective total dose of penicillin in the treatment of syphilis is 1,200,000 units.

It was thought the addition of spirochetostatic and spirocheticidal drugs to penicillin schedules might have value. For instance, what effect would bismuth have if it were added to a penicillin schedule? What effect would the addition of arsenic have? Schoch[2] used a penicillin-bismuth combination, which consisted of 1,200,000 units of penicillin for a period of a week (20,000 units every three hours for seven and one-half days) and 5 injections of 0.2 gm. of bismuth. If his results shown in Figure 2 are compared to those of 1,200,000 units of penicillin alone, penicillin with bismuth would seem to be the better. However, there are several peculiarities of this curve which I think need discussion.

In the first place, relapses occurred a little earlier with the penicillin alone, but as time elapsed it was noted that the failure rates shown in both groups tended to approximate each other. When this chart was first compiled, I projected these two curves and found that at the end of approximately eighteen months they came together.

In other words, since bismuth is a spirochetostat-

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Presented November 10, 1948, before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio.

ic drug, it slows the time of relapse, but the eventual outcome is no better than that of penicillin alone. When the patients, used to compile these curves, had been followed long enough, the two curves came together at the end of sixteen rather than eighteen months. Actually then, the addition of 5 injections of bismuth subsalicylate, during the week of penicillin therapy, added nothing to the curative rate of penicillin alone.

Thomas[3] at Bellevue Hospital in New York has been interested in the combination of penicillin and arsenic. His method of treatment consists of a total dose of 1,200,000 units of penicillin plus the daily injection of 40 mg. of arsenoxide or a total of 320 mg. of the drug. As shown in Figure 3 with penicillin alone the failure rate represented by the solid black line is approximately 29 per cent in eighteen months; with penicillin plus arsenoxide the failure rate is approximately 19 per cent in a similar length of time.

There is no doubt that 1,200,000 units of penicillin plus arsenoxide has a lower failure rate than the same amount of penicillin alone. However, the daily injection of 40 mg. of arsenoxide is toxic; it frequently produces fever, and has been responsible for 1 death in about 2,500 patients from hemorrhagic encephalitis. The morbidity and mortality of the combination of arsenoxide and penicillin should be considered. Furthermore, 1,200,000 units of penicillin is the minimal effective dose, and perhaps 2,400,000 units or 3,600,000 units of penicillin used alone as a total dose might give figures approximating the combination of arsenic and 1,200,000 units of penicillin.

ARTHUR C. CURTIS

ACCEPTABLE SCHEDULES

From these studies one can derive several effective programs, or can use combinations of them now used by other clinics. The following are acceptable schedules:

1. 40,000 units of soluble penicillin are injected intramuscularly every three hours for 60 doses (2,400,000 units).

2. 80,000 units are administered every three hours for 30 doses (2,400,000 units). It is interesting to compare this second schedule with the first. The single dosage is doubled in the second, but the time required for treatment is reduced by one-half, so it becomes approximately a three and one-half or three and three-quarter day schedule. Results with each of these two schedules are identical.

3. 20,000 units of penicillin are given every three hours for 60 doses and 40 mg. of arsenoxide daily for eight days (Evan Thomas plan).

4. 20,000 units of penicillin every three hours for 60 doses are combined with 5 injections of 0.2 gm. of bismuth (Arthur Schoch plan). There is no evidence that the addition of bismuth actually improves this schedule.

5. A regimen used by the United States Public Health Service is 30,000 units of penicillin every three hours for 60 doses, 40 mg. of arsenoxide every other day, and 3 injections of 0.2 gm. of bismuth subsalicylate; in other words, a combination of the Thomas and the Schoch systems. This method of therapy has proved adequate but has some toxicity due to the arsenicals used.

6. A new regimen introduced by Mahoney[4] consists of giving 40,000 units of penicillin every two hours for 85 doses. It was initiated because if one does blood penicillin determinations when soluble penicillin is being injected, demonstrable amounts of penicillin are minimal or absent between the second and the third hour after injection. For that reason, Mahoney used two-hour injection intervals, giving a total of 3,400,000 units of penicil-

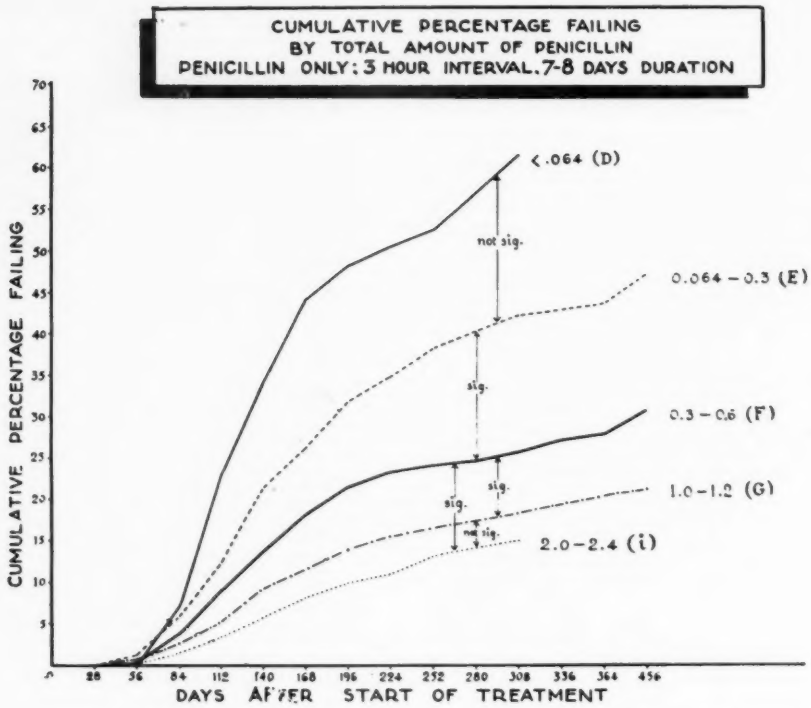

Figure 1. This chart illustrates the failure rates with various total doses of penicillin (aqueous) varying from 64,000 units to 2,400,000 units given every three hours for seven to eight days. There is no significant difference between 1,200,000 and 2,400,000 units, and the minimal effective total dose of penicillin in the therapy of syphilis is, therefore, 1,200,000 units.

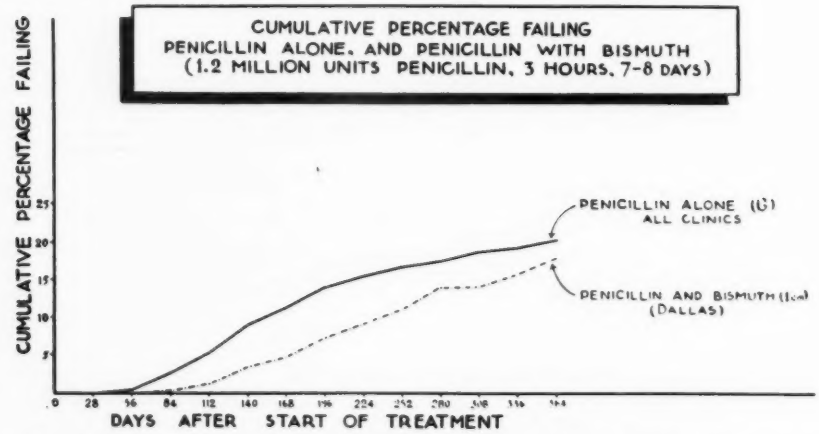

Figure 2. A comparison is made here between the failure rates occurring with 1,200,000 units of penicillin alone and 1,200,000 units of penicillin plus five injections of 0.2 gm. of bismuth (Arthur Schoch plan). The two curves come together at the end of sixteen months, so that bismuth only slows the time of relapse.

lin, but in seven and one-half days. To date his cumulative failure rate is lowest of any regimen.

7. An excellent ambulatory regimen is penicillin in peanut oil and beeswax or procaine penicillin G.[5] Both are usually given in doses of 300,000 units a day for ten to sixteen days with a total dosage of 3,000,000 to 4,800,000 units. This regimen has now been followed long enough to interpret its results, and there is no doubt that, as an outpatient procedure, it is valuable and compares favorably with all other treatment plans used.

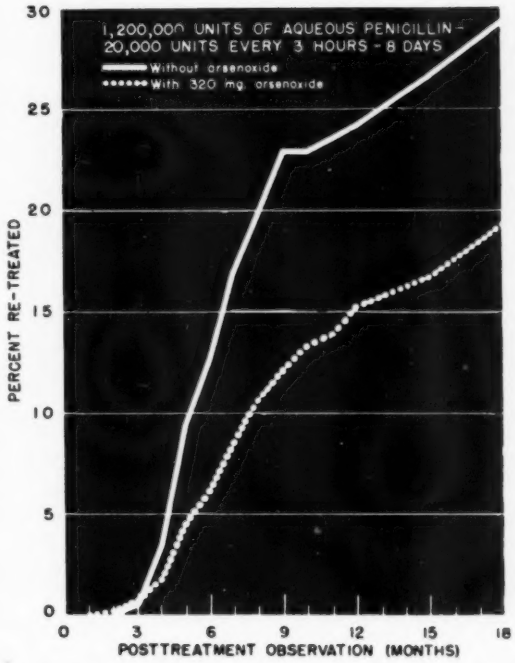

Figure 3. In this chart the failure rates occurring with 1,200,000 units of penicillin with and without 320 mg. arsenoxide are compared. There is a definitely lower failure rate at the end of eighteen months with the 1,200,000 units of penicillin plus arsenoxide (Evan Thomas plan).

FIGURE 4 is interesting because it illustrates a problem in the management of syphilis that should be emphasized more. The data shown by this figure are derived from a compilation of 656 patients with the various types of early syphilis and a projection of the results of their treatment with 2,400,000 units of penicillin as a total dose. If a patient has a seronegative darkfield positive primary lesion, the chances of cure are nearly 100 per cent. If a patient has a seropositive darkfield positive primary lesion, perhaps only two to fourteen days longer in duration of infection, the chances of curing that patient on the same schedule have been reduced about 10 per cent. Then again, if a patient has syphilis in the secondary stage, perhaps a month longer in duration, the chances of cure have been reduced by 28 per cent.

It should be emphasized that the earlier we make the diagnosis in primary or secondary syphilis and the sooner we begin its treatment, the better chance we have to effect a cure.

After treatment of patients with early syphilis, how long should they be followed? If a treatment failure occurs, when will it occur? Figure 5 shows when relapses occurred in 76 patients who had blood tests done at monthly intervals. One finds that a few cases relapse as early as one month after treatment has been completed. Most of the failures occur four months post-treatment, but they do occur as long as six, eight, or ten months post-treatment. Experience, as well as accumulation of figures of this type, has shown that if a patient becomes seronegative at the expected time and maintains seronegativity for a year, that patient can be assured the disease is clinically cured.

Figure 6 shows several things of interest. If a patient is seen with early syphilis who has a quantitative serologic test of 20 units, he will become seronegative in a much shorter time than the patient who has a quantitative test of 80 units. Some patients' serologic tests will decrease in titer to near negativity only to increase later or relapse. Other patients obtain little benefit from penicillin, with only a slight drop in the serologic quantitative titer after treatment.

Relapses may be serologic if only the serologic titer rises, or they may be clinical with a new outcropping of infectious lesions. Occasionally there are patients seen in whom the serologic titer reverts to seronegativity at about the expected time, remains negative for perhaps one, two, or three months, then reverts to seropositivity again. Solution of this problem is a most difficult one. Has this patient had a period of serologic but not biologic negativity? Did the patient still have some infection which eventually, like the peat-bog fire, breaks through the barrier of clinical observation, or was the patient reinfected?

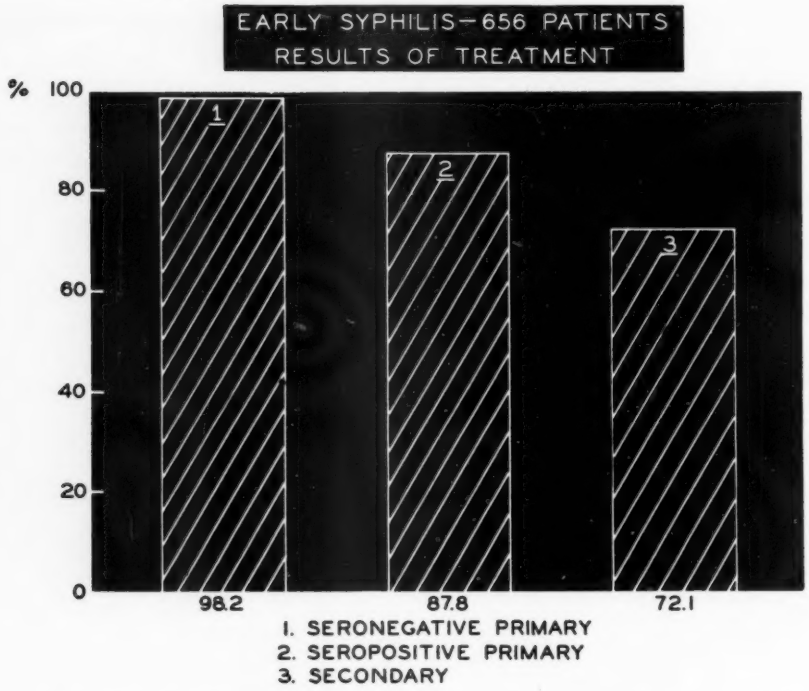

Figure 4. These graphs represent the percentages of cures in the three types of early syphilis treated with 2,400,000 units of penicillin as a total dose. It demonstrates that the earlier the stage of the disease is at the time of institution of treatment, the better the chance to effect a cure.

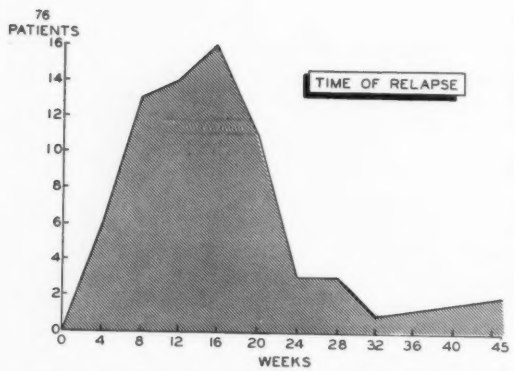

Figure 5. This chart shows the time in weeks at which relapses occurred in 76 patients followed with blood tests at monthly intervals. It is noted that relapses do occur as early as one month and as late as ten months after treatment, but that most relapses occur at four months.

We have no way of knowing how many of our so-called failures are actually reinfections. The only data I know of that might be helpful are those that came from Charity Hospital[6] where a comparative study was made of congenital and acquired syphilis in infants, and the failure rate of that group (which received approximately the same type of treatment an adult would receive) was less than 10 per cent, yet we know an overall group of patients studied in that manner would show an adult failure rate of at least 20 per cent. Perhaps reinfection would account for 50 per cent of what we now call failures.

"PING-PONG" SYPHILIS

The problem illustrated in Figure 7 is aptly called "ping-pong" syphilis. Lawrence, on December 25, 1943, met and cohabited with a young woman in Detroit and was infected with syphilis. Subsequently, Larry returned to the city from which he came where he lived in a trailer camp, and met

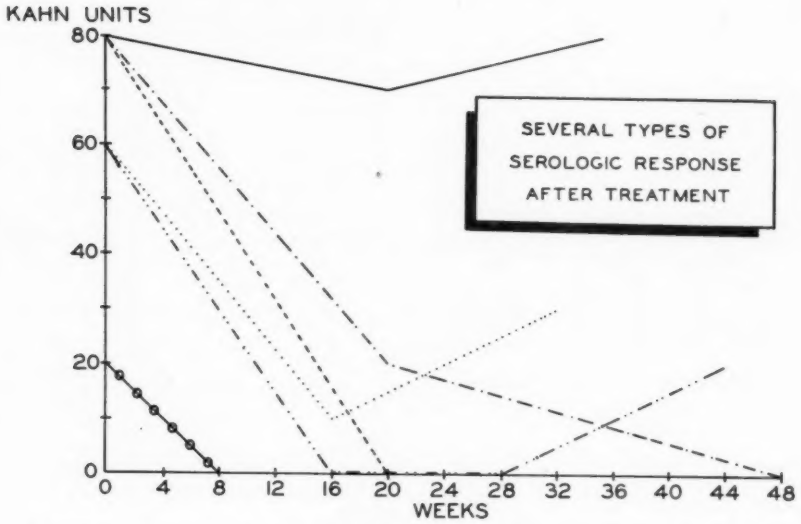

Figure 6. Illustration showing the different types of quantitative serologic responses following treatment. It is seen that the lower the initial quantitative titer, the sooner the return to seronegativity.

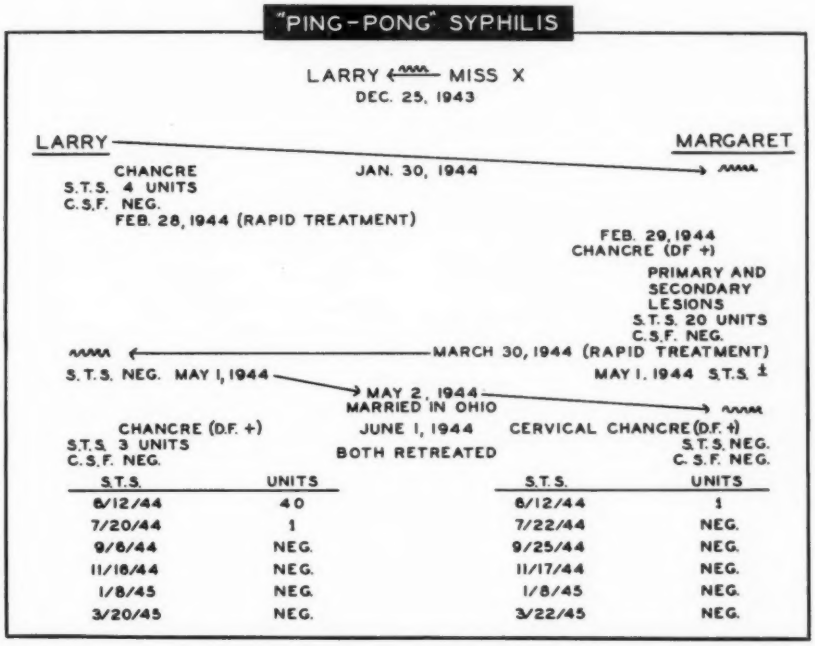

Figure 7. This represents what is commonly referred to as "ping-pong" syphilis. When both were re-treated at the same time, they both became noninfectious.

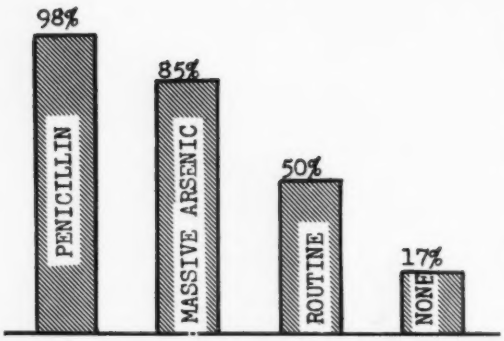

Figure 8. Percentages of satisfactory results obtained by treating syphilitic pregnant mothers with the several methods of treatment and without treatment.

a girl named Margaret. They had sexual congress and Margaret was now infected. On January 30, 1944, Lawrence was seen by the Department of Health in that city and diagnosed as having a darkfield positive chancre. His serologic test was 4 units and his spinal fluid was negative. He did not come to the Rapid Treatment Center until February 28, a month later.

In the meantime Margaret was incubating her disease. When she found out that he was at the Rapid Treatment Center, she went down to the Health Department on February 29 and was found to have a darkfield positive chancre on the cervix. Margaret avoided treatment at this time. In the meantime she developed primary and secondary lesions and her blood test was 20 units.

After Larry's treatment he again had sexual congress with Margaret, who now was in a very infectious state. He influenced her to come to the Rapid Treatment Center, and on March 30, 1944, she received antisyphilitic treatment, but previous to this he had been reinfected with his own spirochetes. On May 2, 1944, they could not be married in Michigan because one of them had a positive serologic test, so they went to Ohio and were married.

On June 1, Larry was seen with a darkfield positive chancre and a positive blood test, and Margaret had a darkfield positive cervical chancre and a negative blood and spinal fluid test. They both said, "Let's get this disease over with," so both were re-treated at the same time and reverted to negativity. One can easily see why two sexually active people who are both infectious can pass syphilis back and forth unless both are simultaneously treated.

SYPHILIS IN PREGNANCY

One of the important problems in the field of syphilis is its effect on the product of the pregnancy. It is known that if a pregnant women has early syphilis and is not treated, her chances of having a normal, healthy baby are only 17 per cent, and 83 per cent of her pregnancies will result in miscarriages, abortions, or syphilized children.[7] With the previously used regimens of arsenic and bismuth therapy, the probability of an infected woman having a normal, healthy child was only 50 per cent (Figure 8). With massive arsenotherapy, a woman's chance of having a normal baby was 85 per cent.[8]

In more than 150 reported cases treated with penicillin, only 2 per cent of the children of such pregnancies, regardless of the trimester in which the penicillin was given, were infected.[9] Therefore, an infected woman today receiving an adequate course of penicillin sometime during her pregnancy, and followed thereafter carefully at monthly intervals with quantitative serologic tests, has a 98 per cent chance of having a healthy, normal baby.

That brings us to a consideration of the attributes of an ideal drug for treatment of syphilis in pregnancy:

1. A drug with a high spirocheticidal index but with no serious toxic effects. Penicillin comes much closer to that than any other known drug.

2. One which prevents transmission of the disease from mother to fetus, or, if transmission has occurred, produces resolution of the process in the child in utero regardless of the stage of pregnancy in which the treatment is given. We have definite evidence that infected children in the uterus have been cured of infection by penicillin therapy given to the mother.

3. One which will provide adequate treatment for the mother. Certainly we know now that penicillin will accomplish this.

4. A drug which can accomplish these aims in a very short period of treatment. Previously mentioned treatment schedules show this can be done. For an infected woman late in pregnancy, where time is an element, a course of only three and one-half or three and three-quarter days could be given, and the mother and child would be adequately treated.

CENTRAL NERVOUS SYSTEM SYPHILIS

The problem of the best treatment for central nervous system syphilis is not yet fully answered. We have now studied approximately 800 patients with some form of central nervous system syphilis who have received one of two forms of therapy[10] (Table 1). One group received penicillin alone, given in doses of 40,000 units every three hours for 100 injections, or a total of 4,000,000 units,

TABLE 1

TYPES OF CENTRAL NERVOUS SYSTEM SYPHILIS TREATED WITH PENICILLIN AND MALARIA AND PENICILLIN

NEUROSYPHILIS	ONE-YEAR GROUP			TWO-YEAR GROUP		
	CASES	TREATMENT		CASES	TREATMENT	
		PENICILLIN	PENICILLIN & MALARIA		PENICILLIN	PENICILLIN & MALARIA
TYPE	NUMBER	NUMBER	NUMBER	NUMBER	NUMBER	NUMBER
Asymptomatic	26	19	7	8	6	2
Meningovascular	20	12	8	15	9	6
Tabes dorsalis	63	37	26	25	19	6
Taboparesis	43	17	26	21	8	13
Paresis	71	23	48	35	13	22
TOTALS	223	108	115	104	55	49

TABLE 2

RESULTS OF TREATMENT OF 223 PATIENTS HAVING SEVERAL TYPES OF NEUROSYPHILIS WITH PENICILLIN AND MALARIA PLUS PENICILLIN FOLLOWED FOR ONE YEAR

APPRAISAL	TREATMENT	IMPROVED		UNCHANGED		WORSE		TOTAL NUMBER
		NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	
Clinical (asymptomatic omitted)	Penicillin	70	79	17	19	2	2	89
	Penicillin and malaria	73	69	25	24	8	7	106
Spinal fluid	Penicillin	89	82	16*	15	3	3	108
	Penicillin and malaria	102	89	11**	9	2	2	115

*Includes 6 patients with negative spinal fluid before treatment.
**Includes 1 patient with negative spinal fluid before treatment.

which we now believe is the minimal effective dose (probably 6,000,000 units would be better). The other group was treated by inoculation with therapeutic malaria and allowed to undergo 8 to 12 paroxysms of chills and fever. At least fifty hours of fever of 103.5° F. rectally were sustained. Penicillin in the same dosage, 40,000 units every three hours for one hundred hours was begun with the first febrile paroxysm.

THE following types of central nervous system syphilis have been treated: asymptomatic, meningovascular, tabes dorsalis, taboparesis, and paresis. Table 2 shows the results in 223 cases followed for one year, and Table 3 the 104 cases followed for two years, after the use of one or the other form of therapy.

An appraisal of these patients as far as clinical findings are concerned shows what seems to be a difference in favor of penicillin alone. The difference of 10 per cent in the one-year and 20 per cent in the two-year studies in clinical improvement between the groups that received penicillin alone and the other that had penicillin and malaria probably means only that the latter had more degeneration of the central nervous system. If one considers the spinal fluid changes, which are the only real indices to the course of the disease after treatment, it is evident that these differences disappear and penicillin with therapeutic malaria seems to be more effective. However, 6 out of 16 patients in the one-year group that received penicillin alone had negative spinal fluids at the beginning of treatment. Only 1 out of 11 had this finding in the penicillin and malaria group.

TABLE 3

RESULTS OF TREATMENT OF 104 PATIENTS HAVING SEVERAL TYPES OF NEUROSYPHILIS WITH PENICILLIN AND MALARIA PLUS PENICILLIN FOLLOWED FOR TWO YEARS

APPRAISAL	TREATMENT	IMPROVED		UNCHANGED		WORSE		TOTAL NUMBER
		NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	
Clinical (asymptomatic omitted)	Penicillin	42	86	6	12	11	2	49
	Penicillin and malaria	31	66	11	23	5	11	47
Spinal fluid	Penicillin	47	85	8*	15	0	0	55
	Penicillin and malaria	48	98	1**	2	0	0	49

*Includes 4 patients with negative spinal fluid before treatment.
**This patient had negative spinal fluid before treatment.

Similarly in the two-year study more patients with negative spinal fluid examinations were treated with penicillin alone than those who had the combined penicillin-malaria therapy. Actually then, a third of the former and a half of the latter improved groups were patients in whom one could expect no change. If these patients were removed from the series, improvement after penicillin alone would be approximately the same as that after penicillin combined with therapeutic malaria. In all types of central nervous system syphilis that were considered, one can say that at the end of one year and at the end of two years the changes in the spinal fluid with penicillin alone are approximately the same as when one adds therapeutic malaria to the same regimen.

In examination of spinal fluid three things are of importance: the cell count (total number of lymphocytes), the total quantitative protein, and the quantitative precipitation or complement fixation test. The colloidal gold test is nothing but an expression, by a different procedure, of the protein in the spinal fluid and the relationship of albumin to the globulin in it.

The comparison (Figure 9) of these two groups of patients—those who received penicillin alone, illustrated by the solid line, and those who had penicillin plus therapeutic malaria (dotted line)—shows the similarity of the curves to be striking. A spinal fluid examination done three months after treatment was completed showed both groups had returned to a normal cell count and remained so throughout a year. That same thing is seen in the two-year group, and they have remained normal throughout two years. So there is no difference in the spinal fluid cell count in these patients, whether or not they received therapeutic malaria.

The second comparison, illustrated in Figure 10, is the result of the quantitative protein test. Our top level of normal spinal fluid quantitative protein is 50 mg. per cent, but again, at the end of three months the average of the quantitative protein has become normal in the one-year group and remained so throughout the study; in the two-year group this same fact is noted, and there is no dissimilarity in the curves.

The next graph (Figure 11) shows improvement by comparing the totals obtained by the addition of the first three figures of the colloidal gold test. If the colloidal gold is 5-5-5, the total figure of 15 would be used; if it is 1-2-3, the total figure would be 6. In referring to this graph, it is seen that there are some differences between the two groups in the beginning, but at the end of three months there is a definite break, and the two curves are similar.

In Figure 12, the quantitative Kahn test is used as an index of comparison. If the titer of the test is expressed in units and these totaled, we find that three months after treatment there has been a real drop in the quantitative Kahn test, and the two curves then follow each other closely for two years. By these methods of comparison one is justified in assuming that penicillin alone is an excellent remedy for the treatment of the various types of central nervous system syphilis.

The only types of central nervous system syphilis in which we are hesitant to express ourselves on the value of the two methods of treatment are in paresis or taboparesis.

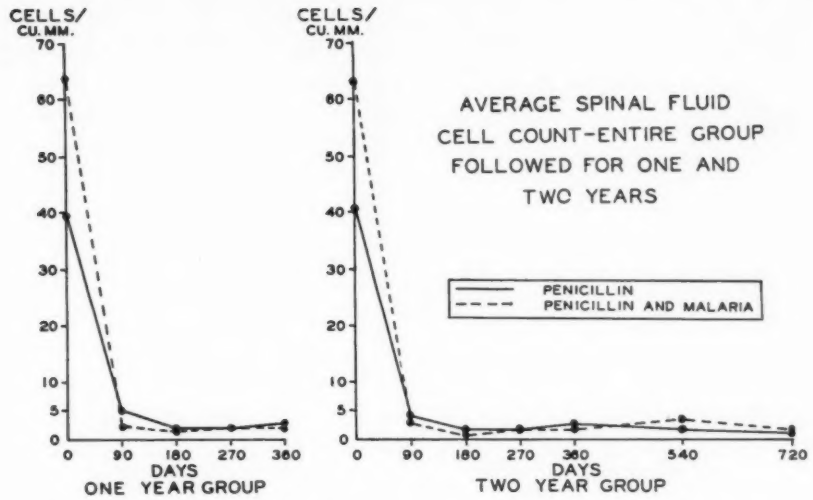

Figure 9. Comparison of the effect on the spinal fluid cell count achieved by penicillin and penicillin plus malaria in the entire group of cases with neurosyphilis. It will be noted in Figures 9, 10, 11, and 12 that although the average figures for the penicillin plus malaria group before treatment was higher than for the penicillin alone series, after ninety days the curves approximate each other.

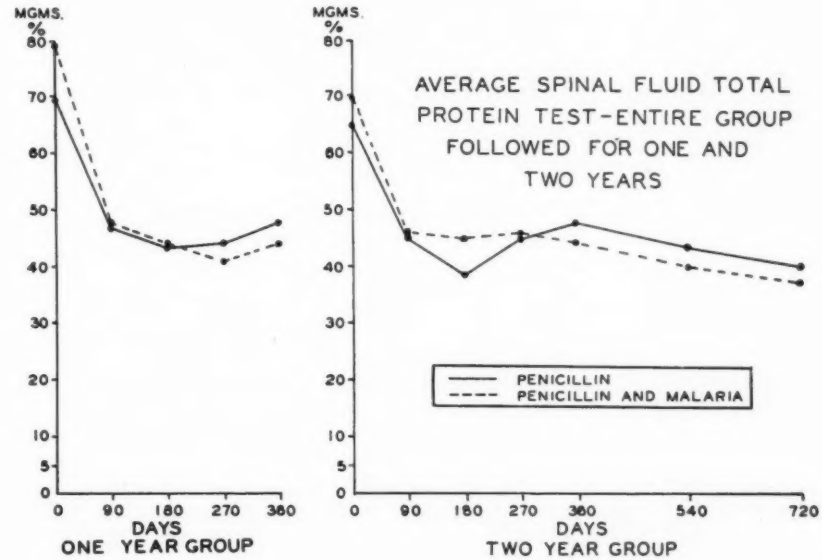

Figure 10. Comparison of the effect on the spinal fluid total protein achieved by penicillin and penicillin plus malaria.

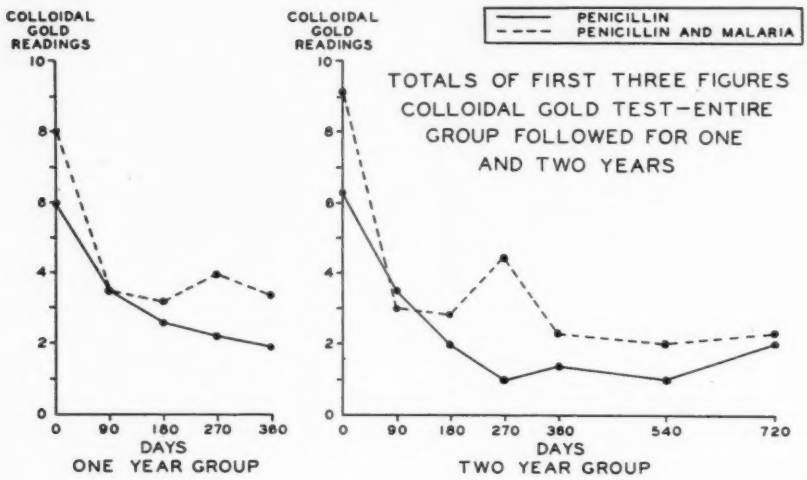

Figure 11. Comparison of the effect on the totals of the first three figures of the colloidal gold test achieved by penicillin and penicillin plus malaria.

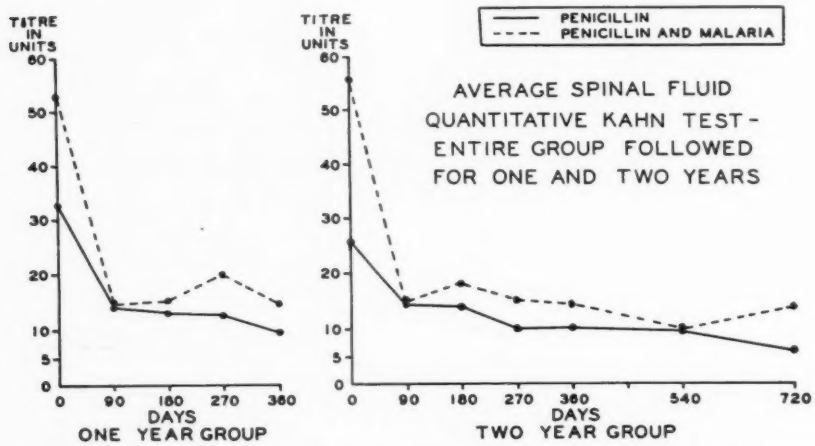

Figure 12. Comparison of the effect on the spinal fluid quantitative Kahn test achieved by penicillin and penicillin plus malaria.

Table 4 illustrates the fact that in paresis at the present time there is a difference between 81 per cent improvement in the spinal fluid with penicillin alone and 97 per cent improvement with penicillin and malaria. This difference seems to be a real one at the end of two years' observation. Whether this difference will persist after a longer period of observation remains to be proved.

In a total of 539 patients with neurosyphilis who have been treated with penicillin alone or penicillin and malaria, 223 were observed for one year and 104 for two years. Patients with asymptomatic neurosyphilis, meningovascular syphilis, and tabes dorsalis responded as well to a regimen of penicil-

TABLE 4

RESULTS OF TREATMENT OF 170 PATIENTS WITH PARESIS INCLUDING TABOPARESIS WITH PENICILLIN AND PENICILLIN PLUS MALARIA

APPRAISAL	TREATMENT	IMPROVED		UNCHANGED		WORSE		TOTAL NUMBER
		NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	
ONE YEAR GROUP—114								
Clinical	Penicillin	27	68	10	25	3	7	40
	Penicillin and malaria	51	69	15	20	8	11	74
Spinal fluid	Penicillin	34	85	6	15	0	0	40
	Penicillin and malaria	65	88	7	9	2	2	74
TWO YEAR GROUP—56								
Clinical	Penicillin	13	62	6	29	2	9	21
	Penicillin and malaria	23	66	8	23	4	11	35
Spinal fluid	Penicillin	17	81	4	19	0	0	21
	Penicillin and malaria	34	97	1	3	0	0	35

lin alone as to one of penicillin and malaria. This response was apparent in both the clinical and the spinal fluid evaluation.

Patients with paresis or taboparesis (they have to be considered together because the prognosis is the same) responded as well in the clinical evaluation of their symptoms to penicillin alone as they did to the combination of penicillin and malaria. The latter regimen obtains a little more improvement after two years as regards spinal fluid improvement. A longer period of post-treatment observation seems indicated before any final conclusion can be drawn regarding the efficacy of penicillin alone in the treatment of this group.

Lastly, the response of patients with the several types of neurosyphilis seems to be more rapid when the combination of penicillin and malaria is used. Even in taboparesis and paresis there are indications that penicillin therapy alone will eventually prove to be as effective as its combination with malaria. Penicillin therapy alone is certainly a far less hazardous procedure.

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DIAGNOSTIC CLINIC

DIFFERENTIAL DIAGNOSIS BETWEEN

Malignant and Benign Breast Lesions

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I DO NOT know whether you take the medical or the surgical approach in the differential diagnosis of mammary lesions. There is a school of surgery, passing out of existence, I think, in which there is very little interest in either the clinical or symptomatic difference between benign and malignant tumors. That school holds that if you find a breast lump you take it out and the pathologist tells you what it is and what to do and there is no clinical distinction of consequence. There is something to be said in favor of this, because at times it is difficult or treacherous to be guided by clinical considerations.

I might preface my remarks, therefore, by saying that in the last analysis the distinction between a benign and a malignant breast tumor is one that has to be made on the excised tissue through pathologic examination.

There is this factor, however. If you persist in excising benign lumps that recur regularly, you are going to lose the confidence of your patient, and the modern school that does make a clinical distinction is going to take over.

I shall cite just one example. We had a nervous patient who, at the age of 34—about fifteen years ago—had a nodule in the upper outer quadrant of her right breast. We removed it because she almost went into hysterics when she found the lump. It was an area of chronic cystic mastitis that we call adenosis or Schimmelbusch's disease.

Following removal, the mass would come and go, and the patient was treated with progesterone. After five years, she had another definite lump at the same site. I was out of town and my colleagues removed the second lump. The pathology was identical to that of the first nodule.

Ten years after the second operation this patient came in for hysterectomy and had another lump in the same area; when we performed the hysterectomy we removed the third tumor. Again it proved to be the same type of chronic cystic mastitis. Before the patient left the hospital the lump was back in the same site. So there were four masses in fifteen years, at the same site, and it had come and gone many other times. She would have had altogether 14 operations if we had relied entirely upon surgery to tell us the difference.

To make a clinical distinction between benign and malignant breast tumors you must first take a history. There are only three things of importance: (1) the age of the patient; (2) the menstrual and marital history, and (3) the history of the breast itself, whether there has been nipple discharge or previous operation, or whether she has nursed or had abscesses or other difficulties.

Age is of some importance inasmuch as carcinoma of the breast is rarely seen before the age of 30, but it does occur after the age of 26; it actually becomes scarce below the age of 25. There are a few cases on record in children or adolescents, but these are exceptional.

As regards marital and menstrual history, do not forget to ask the patient about her menstrual periods and find out if she is pregnant. Many mistakes are made in overlooking an early phase of pregnancy. Pregnancy enhances the vascularity of the breast, increases the rate of growth of fibroadenoma, and causes the disappearance of cystic mastitis after the third month. It is surprising how many doctors can examine the breast and not know the patient is pregnant; breasts do indicate pregnancy after the fifth week.

Pregnancy is also important, because pregnancy

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Presented November 12, 1948, before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio.

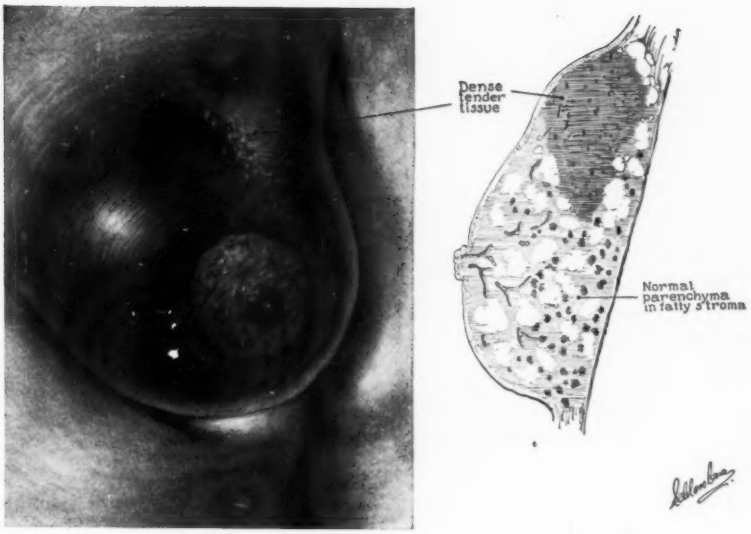

Figure 1. *a.* Drawing to illustrate the characteristics of mastodynia on palpation. Affected tissue is raised, granular, tender, and has ill-defined margins. *b.* Drawing of cross section of same breast.

(Figures 1, 2, 3, 7 and 8 are reproduced from: Geschickter, "Diseases of the Breast," published by J. B. Lippincott Company.)

Figure 2. Drawing to illustrate the characteristics on palpation in adenosis. The breast contains multiple shot-like nodules and has a definite edge when grasped between the fingers.

Figure 3. Characteristics on palpation of cystic disease. A tense, spherical, movable tumor is felt in an adipose breast.

and lactation make a carcinoma of the breast practically a hopeless disease and contraindicate surgery as a rule.

It is important to consider whether your patient is in her teens, or twenties, or toward the menopause. We like to record the history of the menopause. We want to know about the menstrual periods. In chronic cystic mastitis they are irregular, either too close together or too far apart. With cysts of the breast, periods are apt to be skipped because the patient is either approaching or has just gone through the menopause.

As regards the history of the breast itself, we used to say once a cyst always a cyst, but that is not true. Schimmelbusch's disease or adenosis, cysts, or any form of chronic cystic mastitis that comes and goes can occur in middle life and then in the forties the patient can have a carcinoma. The previous presence of chronic cystic mastitis in the breast does not rule out the possibility of cancer.

Nipple discharge is an important observation. If it is milky or serous it usually has no bearing upon the diagnosis unless this is the patient's chief complaint. The only thing that discharge from the breast means, if it is not bloody, is an increased chance of infection to the ducts. With infection periductal mastitis occurs. Many surgeons remove the breast for a simple periductal mastitis. Usually this is present in women toward the menopause who have borne children, but about 5 per cent of the patients are virgins in early adulthood. I have introduced the term virginal periductal mastitis, and have been able to save a good many breasts

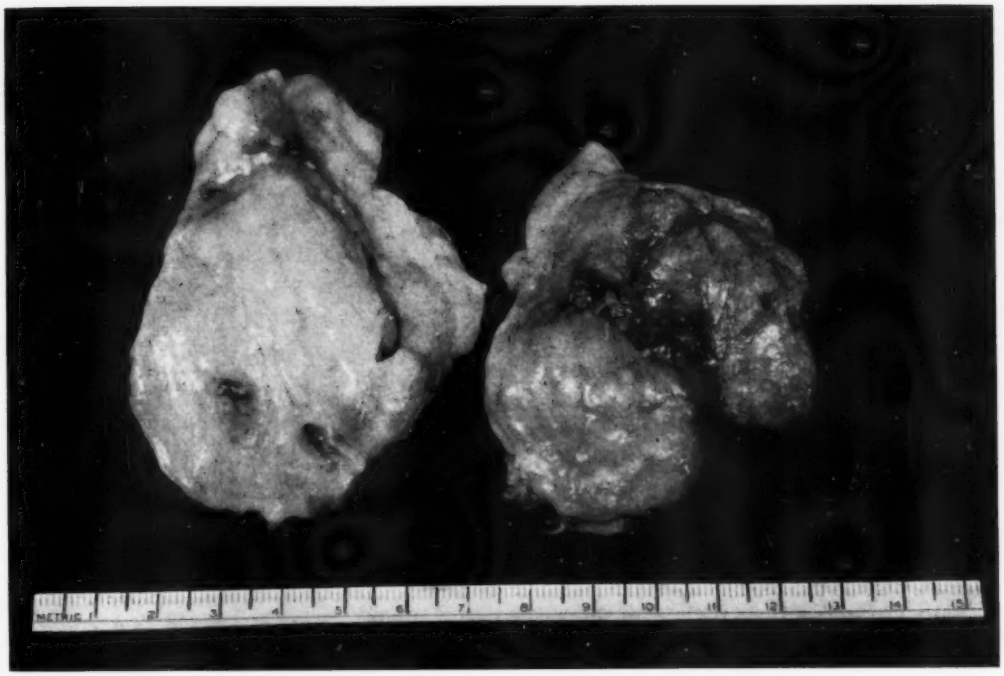

Figure 4. Fibroadenoma. This is a rubbery, firm growth for which excision is both treatment and diagnosis.

by pointing out to surgeons that this type of lesion does occur in girls with a rather characteristic clinical and pathologic picture.

Having taken the history, the patient goes into the examining room. There we inspect the breasts. One breast is often larger than the other; the two breasts are rarely exactly the same; that is usually immaterial. We inspect the breast as the patient assumes a sitting position and elevates the arms slowly over her head. This is a very important procedure because in the presence of malignant tumors the two nipples will not move symmetrically and the breast with the malignant lesion will tend to hug the chest wall or move higher. While we are inspecting the breasts, we watch for any dimpling or retraction as the arms are moved. Then we might compress the breast slightly from the side with our hands to see if any dimpling is brought out.

The nipples are carefully inspected. Unfortunately, about 10 per cent of all cases will have a congenitally retracted nipple. When you see such a nipple you do not presume that it is a sign of cancer; you ask first. A lot of retracted nipples are either due to the fact that the nipple pouch has not everted or the patient was the firstborn in the family, was a little late coming, and therefore had witch's milk in the breast with mastitis neonatorum. Recently acquired retraction of the nipple, however, suggests malignancy, although it occurs also in periductal mastitis.

After inspecting the breast, we proceed to transillumination. This is a valuable procedure. All that is required is a flashlight and a dark room. We transilluminate by putting the light under the breast and look for shadows and the residual effects of any previous infections or operations. It is important to know that if an operation has been carried out on the breast, the scar and inflammation will remain dark for a period of two to four months. If a woman has had an infection of the breast, transillumination is a good guide because you will find a dark residual area and can tell when the inflammation is subsiding by the darkness

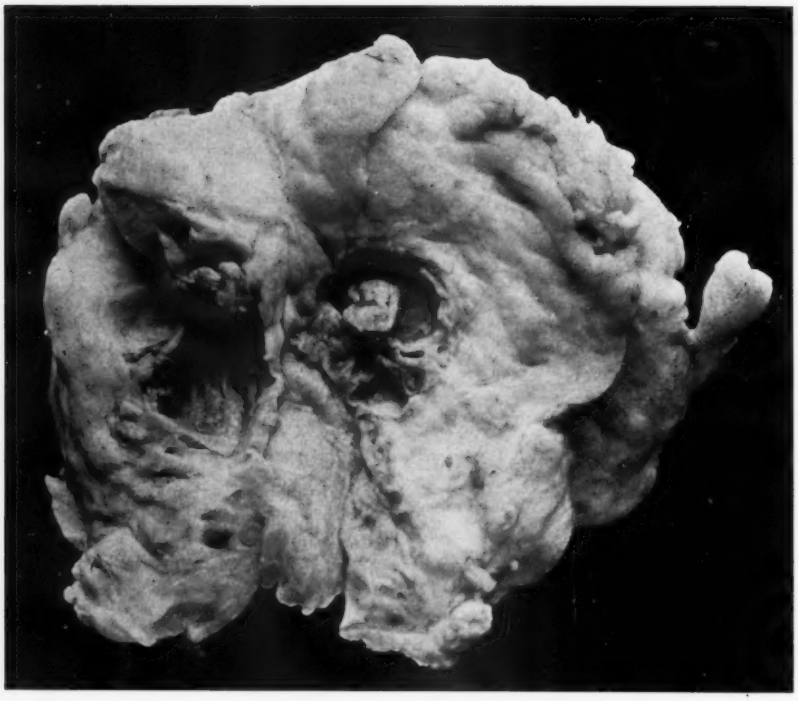

Figure 5. Intracystic papilloma. A gross specimen of the cyst inside the blood-filled cavity is shown here.

around the infected area and its gradual decrease in size.

Transillumination is also of value for bleeding within the ducts in the presence of papilloma. All cancers do not cast a shadow, but a large tumor does. If it is dark and over the size of a nickel it is apt to be malignant. If it is under the size of a nickel and casts a shadow it is either a papilloma or a carcinoma.

We have inspected and transilluminated; now we are going to palpate. This is the most important part of the examination. We palpate either with the palm of the hand or the tips of our fingers. The method is immaterial provided the woman is lying down and you are palpating the breast against the chest wall and are not pinching it, but gently pressing it.

We find that malignant tumors are easily felt except in obese breasts. It is harder to feel a tumor in the lower hemisphere of the breast than it is anywhere else. Bear that in mind. It is always well to ask the patient when you get through, "Have you felt any lumps in the lower portion of your breast?" I have seen experts overlook tumors by palpation which were on the under surface of the breast. Be sure that you are not feeling a rib or the costochondral junction, as this is a possible source of error.

In palpation the malignant tumor jumps up to meet the finger because of the atrophy of the overlying fat. It is hard or irregular. The benign tumor slips away from the finger and is rather indefinite, as a rule, except in fibroadenoma and in cysts. In a fibroadenoma there is a resilient feel and in a cyst there is a fluctuant feel.

Never fail to palpate the margins of the breast and also axillae for metastatic nodes. Remember that all nodules in the breast are not necessarily mammary nodules. We find lipomas from the fat, and also in the lateral portions of the breast we will pick up lymphomas because there is in some individuals a lateral pectoral node that is in the mammary fat.

We are now finished with palpation. We rely upon one other procedure. We have a 20 cc. Luer-Lok syringe and a 22-gauge needle. If we suspect

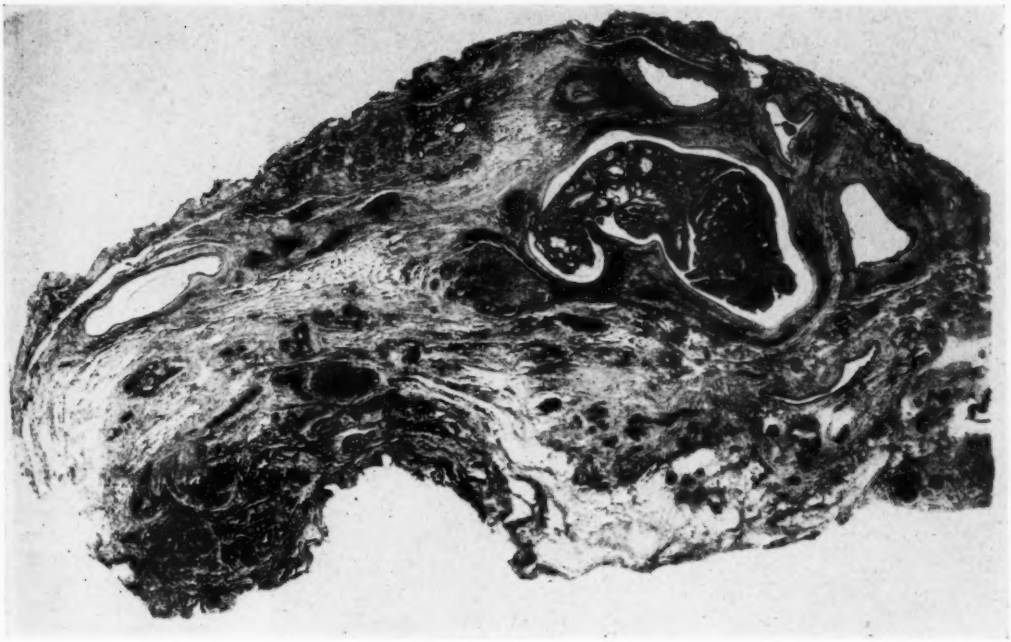

Figure 6. Papilloma associated with malignant invasion, removed by radical mastectomy.

a cyst—not otherwise—we wash the area off with alcohol, grasp the cyst between two fingers, and insert the needle. If we aspirate cloudy cyst fluid from a solitary cyst, the patient is cured and diagnosed at one procedure. It is a most valuable procedure for confirming cystic disease although the cyst in some cases refills after aspiration. If the aspirated fluid is bloody, an intracystic papilloma is present and excision is indicated.

If there is discharge from the nipple, it is always well to examine that discharge microscopically. If it is grossly bloody, you should see red blood cells. Occasionally you find cancer cells in nipple discharge, but this is rather rare. Grumous, dark discharge with amorphous material is found with periductal mastitis.

Figure 1 shows a form of chronic cystic mastitis known as mastodynia. The painful area in the breast is granular and elevated. If it is true mastodynia the patient has tenderness as well as pain. Pain in many forms of arthritis and neuralgia will be referred to the breasts which have no corresponding elevated, granular area that is tender, and then the patient does not wince on palpation. These are merely areas of increased periductal connective tissue due to estrogenic hyperstimulation, and are usually found in firm, well-developed breasts.

The so-called multiple microcystic disease, also known as adenosis, Schimmelbusch's disease, or the nodular type of chronic cystic mastitis is shown in Figure 2. It is bilateral and easily diagnosed on palpation. It usually occurs in women between the ages of 38 and 42, though some young women have it all their lives following puberty. The breasts are usually small. The diagnostic feature is a lateral edge that slips between your fingers when you feel at the periphery. The breast is extremely nodular, like a bean bag.

The disease is associated with irregular menstrual periods, tending to be further apart than normal. As the patient grows older this form of disease actually gives rise to cyst formation. It also has painful elevated tissue similar to that seen in mastodynia. Both these forms of chronic cystic mastitis respond as a rule to progesterone therapy.

Microscopically, the differential diagnosis be-

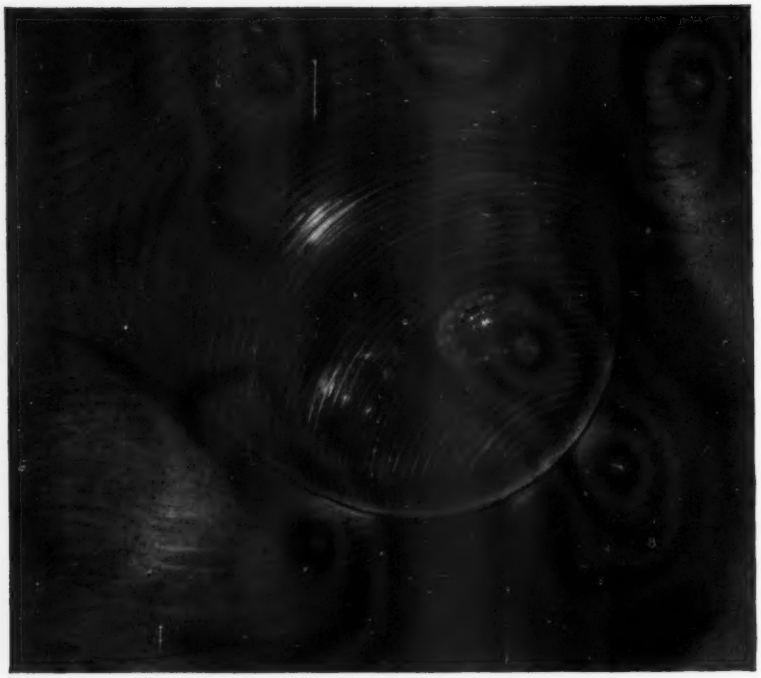

Figure 7. Drawing to illustrate the findings on palpation of infiltrating mammary adenocarcinoma. The tumor is hard, irregular, attached and has the feeling of superficiality because of atrophy of the overlying fat.

tween cancer and this form of chronic mastitis may be extremely difficult, because fibrous tissue invades the lobule rather than the lobule invading the fibrous tissue. This is the so-called fibrosing adenoma that worries pathologists.

The cyst (Figure 3), as I have said, usually occurs toward the menopause in women who have missed one or more periods; it may occur right after the menopause. If you aspirate it and get cloudy or grayish and smoky fluid, the diagnosis is made. Most cases remain well following simple aspiration.

There are two forms of benign tumors. One is the fibroadenoma. This usually occurs in the adolescent or postadolescent period. It is a rubbery, firm growth. The breasts are well dveloped. The tumor does not cast a shadow if it is less than 3 cm. in diameter. In this type of tumor the treatment and the diagnosis are both the same—excision. (Figure 4). The tumor grows rapidly in pregnancy, so if the patient contemplates marriage or pregnancy, removal is indicated to prevent further growth.

The other type of benign tumor is the intracystic papilloma with bloody discharge (Figure 5). Bloody discharge from the nipple is frequently not a sign of cancer; it is more often a sign of benign intracystic papilloma. But, we do not believe a sanguinous discharge can go unheeded without definitive diagnosis, as about 10 per cent of cancers have bloody discharge. We believe in making this diagnosis promptly through surgery. Besides transillumination, we palpate carefully to find out where the bloody fluid is best expressed, and lay down a radial incision along the line of pressure that produces discharge. If, through transillumination, we also pick up the shadow of blood around the papilloma, we know exactly where to make the incision.

We do not believe in simple or radical mastectomies for papilloma, but simple excision. Figure 5 shows the gross specimen of a papilloma in the blood-filled cavity. It may occur within a duct; it can be intraductal or intracystic papilloma, and 10 per cent of these cases undergo malignant change. They are often multiple, and sooner or later you may have to do more than one operation. You may feel better with a mastectomy; the patient won't.

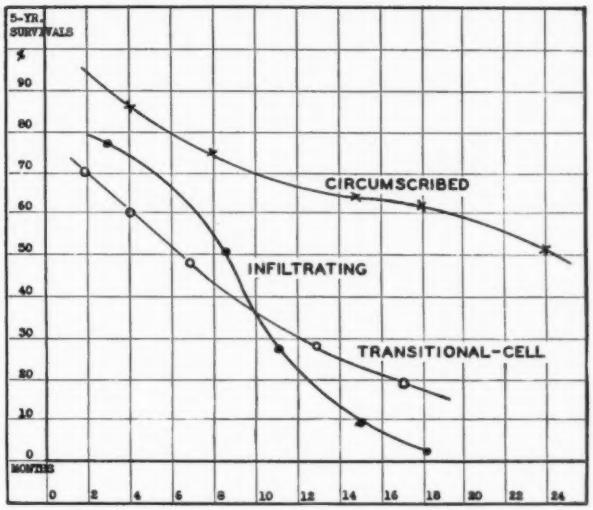

Figure 8. Decrease in percentage of five-year survivals in the different forms of mammary carcinoma in relation to the duration of symptoms.

If the tumor is large and multiple, we do mastectomy or complete operation. In general, simple mastectomy is too much for a benign tumor and too little for a malignant one, so we try local excision once or twice. It is important, however, to have a good microscopic diagnosis.

A case in which the papilloma is associated with malignant invasion, and in which a radical mastectomy was done is illustrated by Figure 6. We always explore bleeding nipples or papilloma of the breast and our treatment is based on the microscopic findings. We do a simple excision for benign tumors, radical resection for those that show invasion.

Now we come to mammary carcinoma. The tendency for the skin to retract, and for the tumor to be small, hard, and to cause atrophy of the overlying fat is the usual thing. The tumor may remain small, even when there is extension, metastasis, and pig-skinning. If you procrastinate the tumor grows to 5 cm., but usually with sound clinical diagnosis a malignant tumor does not go over 2.5 cm. before operation. Even at this size it tends to give metastasis to the lymph nodes of the axilla and to the supraclavicular area.

Mammary carcinoma tends to infiltrate the breast by cords that get into the lymphatics, and to extend very early in the disease. Twenty-five per cent of the cases will have metastasis to the regional lymph nodes before the tumor has passed 1 cm. in diameter. We have found 90 such small tumors with 22 cases involving the axillary nodes in studying 2,000 cases.

The usual type of mammary carcinoma is the infiltrating simple or spheroidal cell carcinoma (carcinoma simplex or scirrhous carcinoma) in which there is marked reaction by the fibrous tissue and the tumor grows in sheets or cords. Because it soon metastasizes to the regional lymph nodes, it is important to discover it by its feeling of induration, by its retraction or dimpling of overlying skin, and by the fact that the woman is usually in her forties. Therefore it is dangerous not to make a definitive diagnosis of any suspicious growth in a patient over 26 years of age and particularly as the patient approaches the menopause (Figure 7).

Transillumination also helps in the diagnosis of malignant tumor of the breast. It is not the stark, sharp shadow that you see with intracystic papilloma or bleeding nipple. In cancer of the breast you see elevation of the nipple on the affected side and its closeness to the chest wall, and some retraction. Early dimpling is difficult to demonstrate but is a most important sign.

The survival of the patient is inversely proportional to the time at which the tumor is discovered (Figure 8). Thus, the most important thing in the diagnosis of malignant tumors is promptness and accuracy. If you pass the sixth month of symptoms, the patient will have a progressively poor chance of cure.

DIAGNOSTIC CLINIC

Testicular Dysfunction

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THERE are three points that I think are almost axiomatic in the treatment of testicular dysfunction. *The first* is that pituitary sex hormone made from pituitary glands of animals has proved to be of little or no clinical value. *The second* is that pregnancy urine extracts are particularly useful in two conditions: (1) cryptorchidism, where testes that might otherwise descend later may be hastened in their descent, giving the physician an opportunity to decide whether or not orchidopexy should be seriously considered; (2) in patients with delayed puberty, where if the testes are sufficiently intact to accept the stimulation of pregnancy urine extracts, male sex hormone will be produced under their effects and sexual maturity brought about.

Pregnancy urine extracts are also useful under similar circumstances to produce growth in stature. This development is the growth spurt of puberty. Pregnancy urine extracts therefore are not useful if the growth delay is due to heart disease or to serious malnutrition, as in badly treated diabetes or chronic kidney disease. Pregnancy urine extracts producing male hormone in this way are no substitute for the growth effects of thyroid, one of the most potent of growth hormones; neither are they a substitute for pituitary growth hormone. Nevertheless, such a spurt, as I will show you later, may occur under the effects of these substances and in some instances such growth may amount to five or six inches per year whereas it had previously been an inch or less a year.

The third chief point in therapy is that testosterone in the usual doses is never useful in the treatment of sterility. It is beneficial for the production of secondary sexual characteristics where the lack of them is due to testicular failure, and is useful in some older men in whom there appears to be a degree of testicular failure.

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Presented November 10, 1948, before the meeting of the Interstate Postgraduate Medical Association of North America, Cleveland, Ohio.

HYPOGONADISM

From a clinical point of view it is fundamental to realize that in childhood hypogonadism is a normal state. All children have hypogonadism, if you wish to look at it from an adult point of view, and therefore the diagnosis of hypogonadism absolutely cannot be made before puberty. In spite of this fact there are instances in which the genitalia may be small, and penile development much lower than normal in cases of infancy or childhood. The fact that testosterone ointment may have caused a response in the most outstanding case of Dr. Hans Lisser does not prove that hypogonadism was present.

In childhood the testicular tubules are represented by solid bands. They have not yet formed a lumen. The interstitial tissue is rather abundant and some of the cells within the interstitial cell mass which looks like fibroblasts are the precursors of the Leydig cells. A normal testis for age 8 years and ten months is shown in Figure 1.

By age 14 the testis has changed tremendously. The tubules have grown to large size. The tubular lumen is forming, and active spermatogenesis has begun.

The pituitary sex hormone—frequently referred to as the follicle stimulating hormone—is at levels below the adult normal level before puberty. It rises slightly up to puberty, and during puberty it quickly rises to within normal adult range, so that all boys we have tested have normal gonadotropins in their urine by the age of 12 and some have relatively high levels by the age of 14. This level of pituitary sex hormone stays at approximately the middle of normal adult range throughout life in most individuals. In some men, however, after the age of 40 or thereabouts, there is a rise to high levels. Among these are the individuals who have

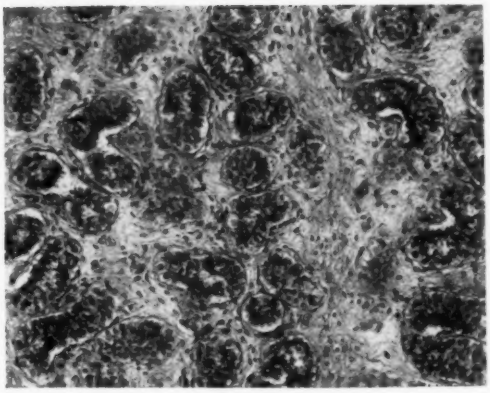


Figure 1. Immature normal: Immature testis from a boy of 8 years. The tubules are represented by small cords. No definite lumens are present. Cells comprising these cords are of a very immature type. The interstitial tissue is great. Mature Leydig cells have not yet been differentiated.

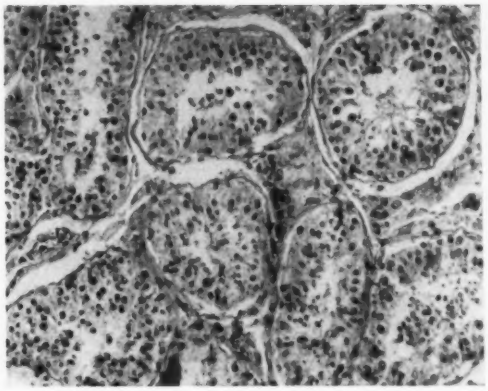


Figure 2. Normal testis in a man aged 26 years. Shows a high grade of activity in the cells of the tubules. Many spermatocytes may be seen near the tubular lumens and here and there spermatozoa find their way into Sertoli cells. Interstitial tissue is relatively less in amount than in the immature testis and large granular nuclei or Leydig cells may be seen.

sterility which in itself may raise the gonadotropic hormone levels in the urine and may not be accompanied by any other symptoms, and some may be those individuals who might legitimately be classed as having a male climacteric.

If the testis hormone in the urine is judged by 17-ketosteroids, which in reality represents excretion products from both adrenals and testes, we may plot a curve on which the first twenty years and each subsequent twenty are not in geometric proportion. In any case, the 17-ketosteroid excretion rises at a slower rate, and stays at approximately 10 mg. per day through the years of 20 to 50, afterwards declining gradually until, in the eighth decade, the levels are at about half the lower limit of the adult normal for earlier years. This is necessary to bear in mind in judging such diagnoses as male climacteric in older men.

We cannot put too much dependence, therefore, on assays for the diagnosis of climacteric, since sometimes high levels of gonadotropins may be found associated with oligospermia but without associated symptoms while in older years 17-ketosteroid excretion levels are rather low normally.

THE main portion of the testis is divided into several functioning parts. There is the Leydig cell with its extreme granulation, large nucleus, and clear area near the nucleus. This is where testosterone is produced. The basement membrane has a cellular portion and a clear hyaline layer. It is extremely important because through this membrane must pass, as far as we know, all the nutriments which reach the testicular tubule. When this membrane is thick or sclerotic there is obviously interference with the nutrition of the interior of the tubules.

Within the tubule there are a series of spermatogenic cells, the spermatogonia, spermatocytes, spermatids, and spermatozoa. These spermatozoa bury themselves within the body of the Sertoli cells and here they stay for an unknown length of time before they are transported down the tubule to be stored in the epididymis. They are not stored in the seminal vesicles. It is in the epididymis that they gain most of their motility.

By adulthood the testis normally acquires an appearance such as is illustrated in Figure 2. The basement membrane is relatively thin, the spermatogenic cells have taken on roughly a layer formation, and there are some sperms buried in Sertoli cells.

Frequently we are confronted with the question as to whether the obesity which is present in childhood is associated with hypogenitalism or hypogonadism. Here we must bear in mind that no

child under the age of puberty can be said to have hypogonadism with certainty unless perchance he is facing it because the testes are known to be severely damaged. One is struck frequently by the fact that a fat boy with this problem is brought by an equally fat father or mother to whom the resemblance is often striking. It calls attention to the likely possibility of familial or congenital traits as well perhaps as family habits of eating.

In a boy at the age of 10 the diagnosis of hypogonadism cannot be made because, even by assays for sex hormones, these measurements should be below normal adult range at this age. At the age of 12 it may be possible to exclude hypogonadism by doing an assay for urinary gonadotropin (pituitary sex hormone, follicle-stimulating hormone). If it is within adult range, which is 13 to 105 mouse units, or if one notes the beginning of pubic hair—an assay method which nature has set up to show us that androgens are being produced—one can predict that puberty will advance normally. If, on the other hand, the testes are abnormally small and the pituitary sex hormone levels already greatly elevated, one then may suspect strongly that primary hypogonadism is present.

There is a good deal of confusion between Frohlich's syndrome, adiposogenital dystrophy, and simple obesity. We take the view that the term Frohlich's syndrome should be relegated to those patients who have pituitary suprasellar neoplasm or Rathke's pouch cyst, when this is associated with obesity and some degree of hypogenitalism, as in Frohlich's original case. We think that adiposogenital dystrophy is a more acceptable term, but it has been pointed out that in many instances simple obesity is the only problem; that can be judged to be present because in such large boys the penis looks particularly small since it is not normal for the penis to grow materially between the age of 1 and the age of 12. In some boys, by the age of 14 if one testis or both testes are abnormally small, or if a testis biopsy shows distinct abnormality of the gland, and if the pituitary sex hormone is shown to be high in the urine, we may decide that we are dealing with a distinct abnormality. Even though pituitary sex hormone levels are high in the urine such individuals may respond markedly to pregnancy urine extract.

Sometimes hypogonadism in older years is congenital. We believe it to be congenital, because as in the patient presented here, the severe eunuchoidism is similar to that seen in Turner's syndrome, stature is low and there may be a suggestion of webbing of the neck. There may also be a group of other congenital anomalies accompanying it. In this patient there was one decidedly small eye, the iris of which measured 7 mm. in diameter, whereas the left eye measured 11. He had a coloboma, facial palsy, definitely deformed palate, and a congenital heart lesion. His testis had an appearance of marked immaturity approximating the normal for age 12.

HERE is an unusual case of an eunuch the like of which I had never seen before, and so far as I know instances of this sort have not been reported in the literature. We have found 3 such individuals. We call them fertile eunuchs. The remarkable part is that he is a thoroughly eunuchoid individual with normal size testicles.

Interestingly enough, excretion of pituitary sex hormone was normal. The microscopic picture of a sample of testis taken at biopsy showed spermatocytogenesis and here and there some spermatozoa being formed, despite the fact that no Leydig cells could be found in the interstitial tissue and it is obvious from a clinical point of view that androgens are lacking.

Pituitary suprasellar tumors and brain tumors in the region of the hypothalamus may cause, in addition to the pituitary cachexia, striking damage to the testes. This is similar to the testis damage which occurs after hypophysectomy in animals, and in them testicular damage is extreme within three weeks.

One such man had a slow-growing oligodendroglioma. The clinical point that made us suspect this was that his first symptom was diabetes insipidus, very seldom seen in suprasellar tumors. This was combined with stupor increasing during the time pituitary failure was advancing. The cells within the testicular tubules had an appearance highly suggestive of those in an immature man or in early youth. There was no differentiation between the types of spermatocytes seen; this is an example of a reversion of the testis toward the childhood level. The basement membrane was noticeably thickened and hyalinized, a change frequently seen in pituitary failure.

In patients with pituitary adenoma there may

be striking lack of sexual development. The 14-year-old boy shown in Figure 3a was 64 inches in height and had a maturity the approximate equivalent of 12 years of age. He had an unusually low metabolic rate, -38 per cent, and 17-ketosteroid excretion was 0.7 mg. per day. In the condition of pituitary failure the 17-ketosteroids are lower than in any condition except two—one is Addison's disease in women and the other is severe myxedema.

We did not know when we first saw this boy that we could depend for diagnosis on an assay for urinary gonadotropin. We know now that levels shown to be 6 mouse units or below may be relied upon. He could not be shown to have a pituitary tumor by means of visual fields or x-ray of the sella turcica, but he was finally operated upon and a tumor was removed. Four months later, whether through the removal of the tumor or by the use of pregnancy urine extracts he changed greatly with decided increase in muscle mass, in fat, increase in size of the genitalia, and evidence of puberty. He has now advanced to a point that would be normal for a 14-year-old. (Figure 3b.)

His testis before operation (Figure 4a) looked like fibrous tissue, and after six months of treatment (Figure 4b) an appearance which would be normal for a 13-year-old was seen.

The testis of an individual (Figure 5) who had severe pituitary failure may be seen in Figure 6. I would like to show you this gentleman. He was losing his eyesight, and twenty-five years ago had a suprasellar tumor and apparently most of his pituitary gland removed, which left him in his present condition. He has marked shrinkage of the testes with all the signs of testicular failure generally and, as might be expected, he has evidences of thyroid and adrenal failure.

The one reason that I wish to present him to you is to call your attention to the fact that under these circumstances a patient gets relatively little help from thyroid or from adrenocortical extract, but relatively a great deal of help from sufficient doses of testosterone. This man has not regained his appearance of ruddiness; his pallor remains; he still has some hypometabolism, but his energy and feeling of well being have increased tremendously with the use of testosterone.

Cryptorchidism has never been shown to be a state of pituitary failure. In such instances we prefer to postpone treatment until the age of 9 or 10 because we see no particular advantage in bringing a testis down by treatment which may come down otherwise. However, I know of no particular harm to be caused by earlier treatment.

Mumps orchitis is one of the commonest causes of eunuchoidism. Sometimes sclerosis of the interstitial tissue is found, and sometimes tubules which are extremely fibrotic and hyalinized are all that remain of the previously normal testis.

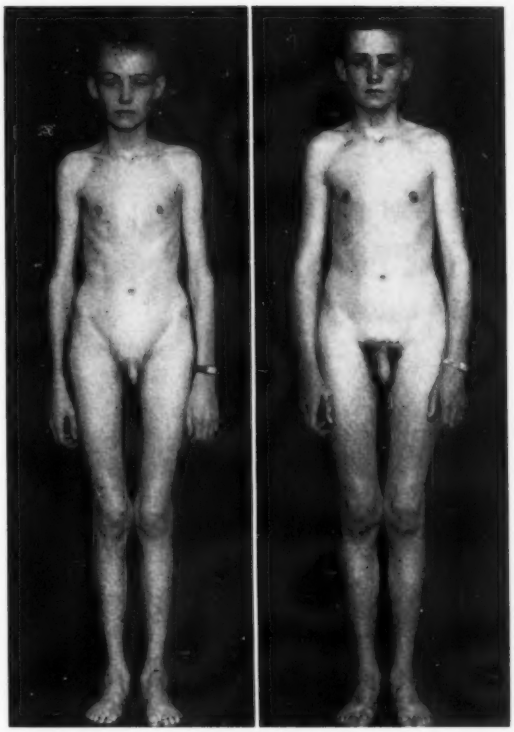


Figure 3*a*. 14-year-old boy with emaciation, pallor, arterial hypotension (90/75), dry skin, mild polydipsia and polyuria, slight enlargement of the sella turcica. B. M. R. -38 per cent. 17-ketosteroids 0.7 mg. in twenty-four hours. Hypopituitarism is evident from the fact that urinary gonadotropins were excreted in amounts less than 6 mouse units in twenty-four hours.

Figure 3*b*. Two months following removal of pituitary adenoma. X-ray treatment to the pituitary region (2,000 r. u. to each temple) and 500 I. U. of chorionic gonadotropin three times weekly. Great improvement in genital and somatic development.

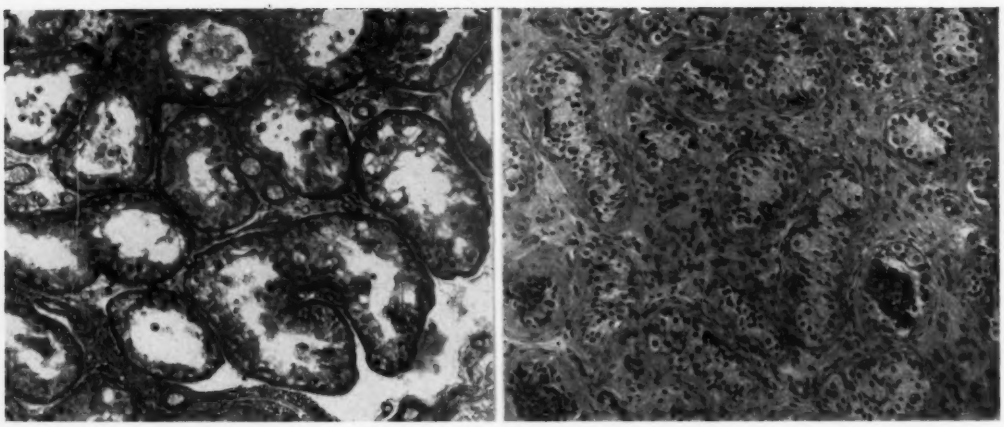


Figure 4*a* (patient in Figure 3). Testis biopsy before treatment. Marked immaturity of tubular structure. Appearance of thickening of the basement membrane and relatively large quantities of interstitial tissue mass.

Figure 4*b*. Testis biopsy after therapy. Note enlargement and maturity of the tubules. The development of some Leydig cells and tubules still is not entirely normal, showing evidence of vacuolization in the gametogenic structure.

In typical eunuchoidism, treatment with pregnancy urine extract is useless because there are not enough Leydig cells to respond. A year of treatment with testosterone in doses of 25 mg. three times a week may be expected to produce striking changes. Erections appear in a few weeks, the voice changes, hair growth and muscular growth quickly appear, and last of all, after one to two years, prostatic growth and beard manifest themselves.

Sometimes gynecomastia appears in conjunction with eunuchoidism, and when it does, the greater the eunuchoidism the less the gynecomastia, as a rule. Gynecomastia is not necessarily associated with inactivity of the testes; perfectly normal testicular activity may be present.

A type of testicular damage we have become acquainted with lately is that caused by stilbestrol. Here again severe gynecomastia appears. Figure 7 shows the testis biopsy of an individual treated for six and one-half months with stilbestrol, and you see the extreme damage to the tubules.

The matter of male climacteric is one which is a very vexing question. Male climacteric, in my opinion, is in itself a misnomer, since there is no evidence that there is any consistent failure of testis function which occurs quickly enough to produce symptoms and may still be considered physiologic. It is a striking fact that some men who are castrated develop no symptoms of consequence. It is also a fact that testes of men as old as 70 and in the early eighties show active spermatogenesis. We think that when this diagnostic problem arises, that if a sperm count can be obtained and it is shown to be entirely normal, it is unlikely that such an individual has male climacteric even though his nervous symptoms or suggestion of hot flashes may suggest it. The volume of semen under such circumstances reflects the effects of circulating androgens.

It seems unlikely that anyone can have male climacteric unless he has a high assay for pituitary gonadotropin. However, in judging this test it is worth while, as mentioned before, to remember that the levels of gonadotropins may be very high without symptoms in individuals who have oligospermia.

If male climacteric is seriously suspected there is little harm, in most instances, in prescribing testosterone. If one gives 50 mg. three times a week for three weeks, the symptoms, if they are due to testicular failure, should be largely controlled. If the symptoms disappear almost completely after the first dose, obviously it suggests

Figure 5. Pituitary cachexia: Age 67. Pituitary failure following excision of a suprasellar cyst twenty-five years ago. Urinary 17-ketosteroids 0.8 mg. in twenty-four hours. Urinary gonadotropins less than 6 mouse units in twenty-four hours. Kepler water excretion test index 1.2.

psychoneurosis. If the control is more gradual it suggests testis failure or that the effect may be purely pharmacologic. It is a striking fact that large doses of testosterone given to women who have inoperable breast cancer give a rather pronounced feeling of well being, no proof, certainly, under these circumstances, of a pretreatment androgen deficiency.

If a man has, or is suspected of having, cancer of the prostate, one obviously does not prescribe testosterone.

Other untoward effects of testosterone are gynecomastia, which sometimes occurs, and if fertility is a problem the sperm count may be forced down by testosterone. Testosterone in doses commonly employed is contraindicated as a treatment for sterility.

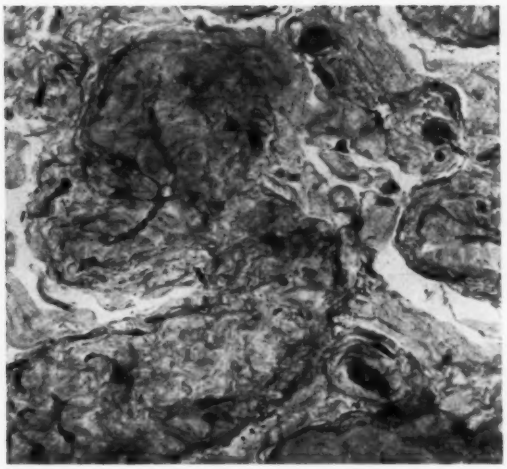


Figure 6 (patient in Figure 5). Testis biopsy showing extreme atrophy and disappearance of Leydig cells, thickening of basement membrane and hyaline changes. Firm masses of sclerotic tissue represent previous tubules.

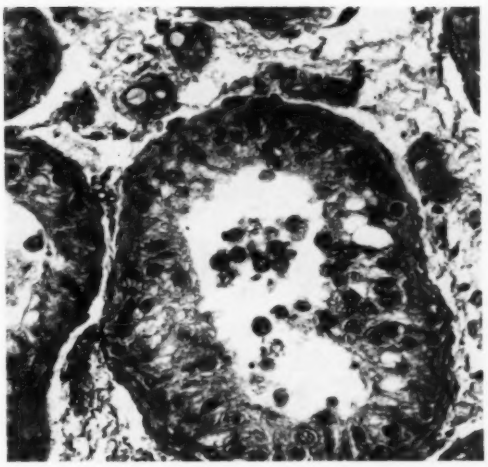


Figure 7. Testis biopsy from a man who had taken 200 mg. of stilbestrol over a period of six months. It is evident that the tubular structure is degenerated. When large doses of stilbestrol are continued for a long time the tubule becomes completely destroyed. Leydig cells appear to diminish in part and later almost disappear.

Essential Hypertension

CLINICAL AND PATHOLOGIC CHARACTERISTICS

HARRISON S. MARTLAND*

Persistent arterial hypertension in which the systolic blood pressure is constantly over 140 and the diastolic over 90 is the most important problem in medicine today, as most of us in the decrescent period of cardiovascular life (over 40 years) will be incapacitated or our normal span of life shortened by this condition.

Primary or essential hypertension comprises some 88 per cent of all cases of persistent arterial hypertension and, in spite of all the various theories and concepts as to its etiology, its real cause is not at present known.

The remaining 12 per cent of persistent arterial hypertension covers a variety of conditions, most of them renal in origin (glomerulo-nephritis, acute or chronic; pyelonephritis, bilateral or unilateral; polycystic disease of kidneys; renal artery occlusions, partial or complete; renal tumors and infarcts; renal amyloid disease; peri-arteritis nodosa of renal vessels; pheochromocytomas of adrenal; and urinary tract obstructions and infections).

Since most of these causes present urologic problems in their diagnosis and treatment, some have advised that everyone with hypertension should be screened by a complete urologic examination, a costly and impractical procedure that would make no appreciable dent in the predominate number of cases of hypertension in which there is no proof of a primary renal lesion as the cause of the hypertension.

Essential hypertension has been divided chiefly by the clinicians into a *benign form* which comprises about 90 per cent of the cases and a *malignant form* which takes in less than 10 per cent of the total cases.

Essential hypertension of the benign type has the following characteristics: Most cases develop between the ages of 50 and 60, and can be clinically divided into mild and severe cases.

Very mild cases show only moderate hypertension with low diastolic pressure; pressure fluctuates and may reach normal during sleep; no albuminuria; electrocardiograms often remain normal; retinal arteries show nothing more than "Copper Wire" appearance; course is very slow and may last for twenty years or longer, and not even shorten to any extent the normal life span; often symptomless and patients in apparent good health until told they have hypertension.

More severe cases in which the hypertension becomes fixed at high levels, often after an insidious onset; dyspnea on exertion; mild to moderate nocturia; morning headaches; vertigo, etc.; albuminuria and slight hematuria often occurs; electrocardiograms are apt to show evidence of myocardial damage due to associated coronary arteriosclerosis and its sequelae; angiospastic retinitis with sclerotic changes in arterioles of disks often occurs; papilledema, however, never develops.

Cause of Death in Benign Forms—About 70 to 80 per cent of deaths are cardiac due to congestive failure or sudden from coronary arteriosclerosis or hypertrophied hearts showing good musculature and minimal coronary arteriosclerosis.

Another 20 to 30 per cent are cerebral usually from apoplexy, cerebral thrombosis, or embolism.

Benign essential hypertension, therefore, is benign only if the patient escapes a cardiac death or a cerebral hemorrhage or softening.

Essential hypertension of the malignant type is characterized by severe retinopathy and renal failure and comprises less than 10 per cent of the total number of cases of essential hypertension. The onset is often sudden with rapid fixation of both systolic and diastolic pressures at a very high level. It becomes a grave disease in a very short time with failing vision, dyspnea, precordial pain, etc. The eye findings are characteristic—extensive retinopathy with hemorrhage, exudation, and intense constriction of arterioles; papilledema develops before signs of renal failure. In the course of a few months renal insufficiency sets in.

Cause of Death in Malignant Forms—Uremia or renal insufficiency is the main cause of death. Fulminating hemorrhagic encephalitis occasionally occurs.

*Chief Medical Examiner of Essex County, New Jersey, and Professor of Forensic Medicine, New York University College of Medicine. Photographs prepared by Dr. Martland and reproduced in *Postgradnate Medicine* through the courtesy of Ciba Pharmaceutical Products, Inc.

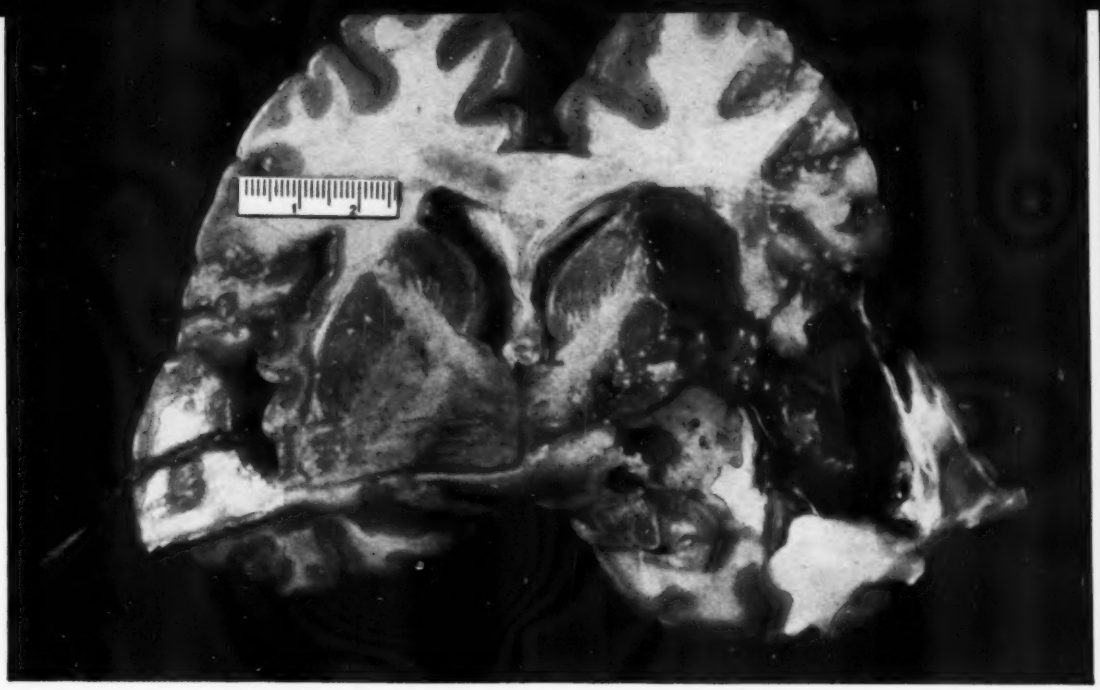


Plate 1—Apoplexy in Right Internal Capsule and Lenticular Nucleus

A large, recent hemorrhage in right lenticular nucleus and internal capsule (quadrilateral space of Pierre-Marie) breaking through to cortex with destruction of outer portion of internal capsule may be noted.

Male, age 58. Left hemiplegia; lived three days in deep coma.

Plate 2—Apoplexy in Left Lenticular Nucleus

A large, recent hemorrhage in left lenticular nucleus external to the internal capsule but compressing it with surrounding edema of white matter may be noted. The brain tightly hugs the cranium, with flattening and smoothing of the convolutions due to increased intracranial pressure also shown.

Male, age 65. Paralysis of right face, arm and leg with flaccidity followed by spasticity, exaggerated reflexes and Babinski. Lived ten days in comatose state.

COMMON LOCATION OF

MASSIVE CEREBRAL HEMORRHAGE (APOPLEXY)

IN ESSENTIAL HYPERTENSION

The two cases shown had ***essential hypertension of the benign type*** as manifested by hypertrophy of the left ventricle and benign nephrosclerosis. Both had extensive cerebral arteriosclerosis.

Such apoplectic hemorrhages are usually due to rupture of arteries in areas of ischemic encephalomalacia caused by vascular thrombosis and occlusion.

The small arteries coming directly off the middle cerebral artery and supplying the region of the lenticular nucleus and internal capsule are most frequently involved.

Sudden death is unusual in apoplexy unless the hemorrhage breaks into the lateral or fourth ventricles.

The almost universal usage of clinicians and interns of the term "Cerebral Accident" on the death certificate to cover such cases is to be condemned and has often given rise to claims for accidental death, double indemnity, etc.

SCIENTIFIC EXHIBIT

Treatment of Infantile Paralysis

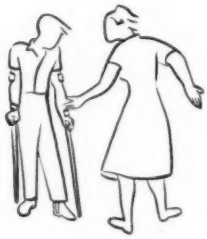
NATIONAL FOUNDATION FOR INFANTILE PARALYSIS

PREPARED IN CO-OPERATION WITH GEORGIA WARM SPRINGS FOUNDATION AND BASED ON TREATMENT METHODS EMPLOYED THERE*

Save life

Prepare for motion

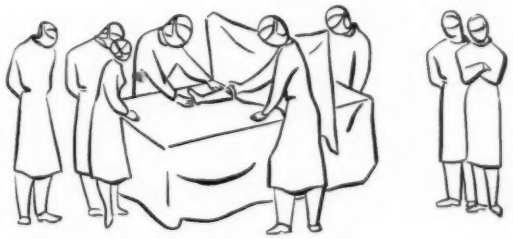
Coordinate and strengthen



Increase functional activity

Evaluate

Return home



Orthopedic surgery

Text prepared under the direction of Dr. Robert L. Bennett

Diagnosis of Spinal Poliomyelitis

1. Acute onset of a spotty segmental weakness ranging from slight paresis to complete flaccid paralysis.
2. With or without previous nonspecific prodrome of one to ten days' duration.
3. No gross sensory changes. Minor and transient paresthesias may be noted in the early stages.
4. Altered deep tendon reflexes in involved segments. These reflexes may be briefly exaggerated; may tire quickly; may be depressed; or may be completely absent.
5. Characteristic, but nonspecific spinal fluid findings. These findings may not be present in the very early stages. May be accompanied by moderate increase cell count (50—250) moderate increase total protein (50 to 150 mgm. per cent).
6. May be accompanied by any combination and degree of motor involvement in medulla and mid brain.

Danger Signs in Spinal Poliomyelitis

1. Respiratory failure due to weakness in primary muscles of inspiration (intercostals and/or diaphragm).
   a. Inability to count to fifteen without taking second breath.
   b. Gradually increasing respiratory rate and depth, but with constant regular rhythm.
   c. Use of accessory respiratory muscles to assist inspiration during periods of minimal activity.

      Spasm in abdominals, erector spinae and intercostals makes inspiration difficult and painful, speeds up fatigue of accessory respiratory muscles.
   d. Unequal (asymmetrical) chest expansion.
2. Anxiety, restlessness and confusion indicate cerebral hypoxia.
3. Strangulation may occur with
   a. Difficulty in swallowing due to retraction of head by painful "spasm" in posterior cervical muscles.
   b. Difficulty in coughing because of weakness in diaphragm and/or abdominals.
4. Severe lower motor neuron damage indicated by:
   a. Early complete flaccidity of entire bodily segment (i.e., shoulder-arm, forearm-hand, trunk, hip-thigh, leg-foot).
   b. Persistent strong and usually painful contraction of muscle groups. This is particularly significant
      (1) When opposing groups are in "spasm."
      (2) When spasm is followed by flaccidity.

Treatment of Spinal Poliomyelitis

1. Complete rest is keynote of treatment in acute stage of spinal poliomyelitis. Complete rest is only possible through measures designed to relieve pain and minimize apprehension.
2. Sedatives (barbiturates) may be used, but only when there is absolutely no evidence of bulbar involvement.
3. The comfort of the patient determines position of the involved segments. A firm (not hard) bed with pillows and sand bags should be used for positioning.
4. Competent nursing (private if possible) helps reassure and quiet patient.
5. Warm, moist fomentations should be used but only over painful muscle groups. Complete hot packing of the patient is rarely necessary and may be dangerous.
6. Warm, moist fomentations, sedatives, massage, and passive motion relieve post cervical "spasm" and assist swallowing.

Bulbar Type

Early recognition and treatment of decreased oxygenation are the most effective means of reducing mortality rate.

Spinal Type

Early accurate diagnosis of acute anterior poliomyelitis reduces mortality rate by alerting the physician to watch for signs of impending danger.

Diagnosis of Bulbar Poliomyelitis

Acute onset of marked anxiety and restlessness with any combination of the following findings:

1. Weakness in muscles supplied by the cranial nerves: Ophthalmoplegia, facial weakness, difficulty in swallowing, change in voice tone, deviation of palate, loss of gag reflex, etc.
2. Disturbances in the automatic control of breathing: jerky, irregular respiration with variations in rate, depth and rhythm.
3. Disturbances in cardiac function: very rapid pulse rate, varying blood pressures with decreasing pulse pressure.

May be accompanied by any combination of the lower motor neuron involvement of spinal cord with or without characteristic spinal fluid changes.

Danger Signs in Bulbar Poliomyelitis

1. Difficulty in swallowing and/or regurgitation of food and fluids.
2. Harsh strident voice tone.
3. Irregular respiratory rhythm with increasing periods of apnea.
4. Varying blood pressures with low pulse pressure.
5. Increasing pulse rate.
6. Extreme anxiety, restlessness and confusion.

Treatment of Bulbar Poliomyelitis

1. Constant observation.
2. Stop all food and fluid by mouth to prevent strangulation.
3. Do not give sedatives.
4. Adequate available oxygen is keynote of entire treatment program.

Provide by:

a. Postural drainage and removal of accumulated saliva by suction to keep air-way free if swallowing is difficult.

b. Oxygen through nasal tube if trachea is free of obstruction.

c. Tracheotomy at earliest sign of tracheal obstruction.

d. Humidified oxygen under pressure through tracheotomy tube if necessary.

e. Mechanical respiration should be used only with failure of respiratory center and increasing weakness in muscles of inspiration, *but* trachea and pharynx must be free of obstruction. (Tracheotomy and/or intubation may be necessary.)

f. Stimulants may be of value in cardiac and/or circulatory failure.

Relieve Pain and Release Tightness

Hot moist fomentations should be used only where needed to relieve pain and spasm.

Physical Therapy and Nursing Services combine in early convalescent stage to make patient comfortable and maintain normal alinement of bodily segments.

Passive movement of involved segments in warm water (98° to 103°) helps relieve pain and tightness.

Before any attempt is made to reestablish coordinate action of the neuromuscular system, free and painless motion of the involved bodily segments must be possible. Persistent pain and limitation of motion not only prevent coordination of muscle action, but also promote development of faulty patterns of motion. *At this critical period every attempt must be made to prevent haphazard movement.*

Relief of pain and release of tightness are usually obtained within the first month after onset. This is accomplished by intelligent medical and nursing care emphasizing comfortable positions of rest, routine changing of position, judicious sedation, application of heat, passive motion of involved bodily segments, and support of weakened segments in normal alinement.

Support Weakness

Semi-sitting position in bed should be permitted early.

Children may require "anti-rotator bars" attached to well fitting shoes to hold weakened extremities in position.

If a corset is used to support a weakened trunk it must be checked frequently. (a. Correct support. b. Inadequate support.)

The basis for all musculoskeletal deformities in poliomyelitis is persistent faulty alinement of bodily segments at rest and/or during activity. Faulty alinement may result from:

(1) Weakness.

EARLY (2) Pain.

(3) Persistent contraction.

a. Neurogenic "spasm."

b. Reflex "splinting."

(4) Faulty patterns of activity due to:

a. Spotty weakness.

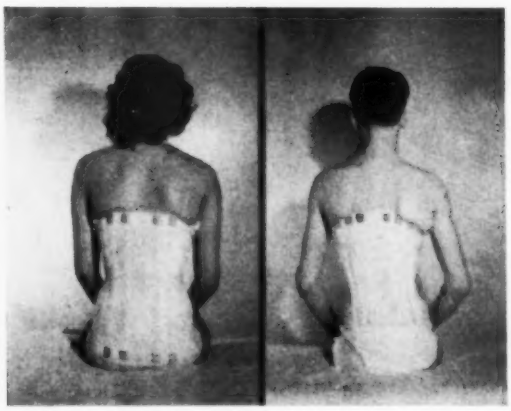
b. Poor coordination.

LATER c. Contractures of muscular, fascial and periarticular structures.

d. Inadequate or improper support of weakened segments.

(5) Inability of fibrous muscle to elongate with bone growth.

When weakness is the cause of persistent faulty alinement, the segment should be maintained in normal position by comfortable and easily removable support. If at all possible, this support should permit functional activity, but with no danger of stretching weakened muscles or placing stress on unsupported bones and joints.



COORDINATE AND STRENGTHEN MUSCLE ACTION

Muscle Strength Testing

Thorough knowledge of functional anatomy is necessary to position bodily segments properly to obtain accurate grading of individual muscles or groups of muscles.

Early grading of muscle strength may not be possible in functional position. This must be noted on the muscle test record (gastrocnemius-soleus standing test).

Final grading of all muscle groups must be based on the function they normally perform (gastrocnemius-soleus standing test).

Accurate muscle strength testing is necessary to:

1. Prescribe and carry out proper muscle reeducation.
2. Determine progress of treatment.
3. Estimate need, time and probable success of orthopedic surgery.

Classification of Muscle Strength

5	100%	N Normal:	Complete range of motion against gravity and full resistance.
4	80%	G Good:	Complete range of motion against gravity with moderate resistance added.
3	50%	F Fair:	Complete range of motion against gravity.
2	20%	P Poor:	Complete range of motion with gravity eliminated.
1	5%	Tr Trace:	Palpable or visible contraction producing no joint movement.
0	0	0 Zero:	No evidence of voluntary contraction.

Coordinate Muscle Function

Restoring coordinate muscle action requires meticulous care by trained physical and occupational therapists. Physical therapy initiates coordinate patterns of motion by teaching the patient to use the "right muscles at the right time." Occupational therapy assists in "setting" basic coordinate patterns of motion through interesting and instructive activities.

All programs designed to restore maximum functional capacity must be based on the premise that the end result will depend not only on the damage to the central nervous system but on what is done with what is left. These patients can never hope to attain normal functional capacity with far less than normal numbers of myoneural units unless each unit is perfectly coordinate in its group action. Restoring coordination is the keystone of the convalescent phase of this program. Unless existing muscle action is coordinated, maximum strength and endurance can never be obtained.

Increase Muscle Strength and Endurance

Strength may be increased by requiring muscle groups to work against heavy loads properly placed to bring out the best effort. Water has no specific medicinal value in polio, but it is an excellent medium in which to carry out assistive, supportive, and resistive exercises. Carefully prescribed and supervised arts and crafts help increase strength and endurance.

Strength is basically the result of a maximum number of myoneural units acting simultaneously to achieve maximum effort. Strength is obtained through activity requiring great effort and therefore repeated only a few times (maximum resistance, minimum repetition).

Endurance is basically the result of a minimal number of myoneural units, acting to achieve the desired activity with a sufficient number in reserve to permit continued effort. Endurance is obtained through repeated activity requiring little strength to perform (maximum repetition, minimal resistance).

No athlete ever needed a coach as badly as a patient with polio needs a skilled therapist.

Both strength and endurance depend on coordination.

Increased Use of Upper Extremities

Increased functional capacity can best be achieved by interesting and stimulating activities. Selected arts and crafts are ideal.

Activity to encourage coordinate use of all bodily segments preferred when possible.

Properly fitted apparatus may be necessary to achieve coordinate function.

In this phase of convalescent care, functional occupational therapy plays a major role. The occupational therapist must not only thoroughly understand coordinate muscle action and recognize faulty patterns of substitution, but also be experienced in the use of assistive and supportive apparatus and be ingenious in devising such apparatus.

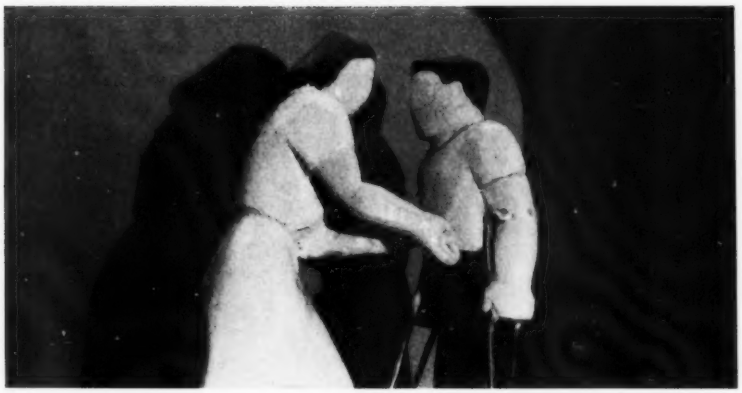
The occupational therapist adapts her knowledge of arts and crafts to the patients' individual needs for increased functional use of upper extremities.

Recreation Therapy

Recreation is an important and necessary part of any convalescent program. As a therapeutic agent, it should be used not only to amuse and pass time, but more specifically to bring the patient in contact with other individuals, stimulate normally directed competition, teach good sportsmanship, and minimize consciousness of physical handicap.

The basic philosophy of recreational therapy is to develop normal personality through individual and group achievement and/or competition. It is well to remember that social rehabilitation must keep pace with physical and mental rehabilitation.

Selected recreation can also be used to increase coordination, strength and endurance.



Walking Reeducation

Walking must follow as nearly a normal pattern as possible. Crutches and/or braces should be used if necessary to support weakened segments and prevent deformity.

In the early and mid convalescent phases of recovery such apparatus should be considered a part of the treatment. If increased strength occurs through activity, apparatus can eventually be discarded.

When severe weakness exists in the muscles of the lower extremities, the muscles of the trunk and upper extremities must be strengthened in preparation for walking with crutches.

Walking can never be considered really practical unless the patient can get out of and into a chair safely and easily without assistance.

After basic patterns of coordination have been established and individual muscles and muscle groups have been strengthened by specific exercises, gradually increased functional activity of the body as a working unit is prescribed and carefully supervised.

In the late convalescent phase of treatment, apparatus may be necessary permanently to support and assist safe activity in a weakened extremity or until orthopedic surgery can restore safe and increased activity without the necessity for apparatus.

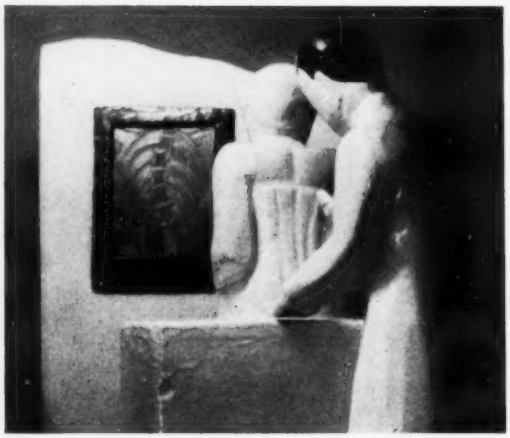
It is well to remember that all patients associate recovery with their ability to walk again. Even the severely involved deserve a chance to try walking until proved impractical.

Functional Capacity

Patients should be evaluated and trained in terms of their ability to return to a normal environment and live happy and useful lives.

The functional capacity of all patients should be evaluated on their ability to cope with the ordinary demands of living in a normal environment. During the middle and late convalescent phases of recovery the patient should be given routine "functional tests" along with the routine muscle tests. These tests begin with an evaluation of the patient's ability to move about in bed and progress through the abilities of eating, personal hygiene, dressing, writing (or typing), locomotion, and so forth.

Occupational testing should also be carried out, utilizing the services of agencies devoted to vocational rehabilitation.



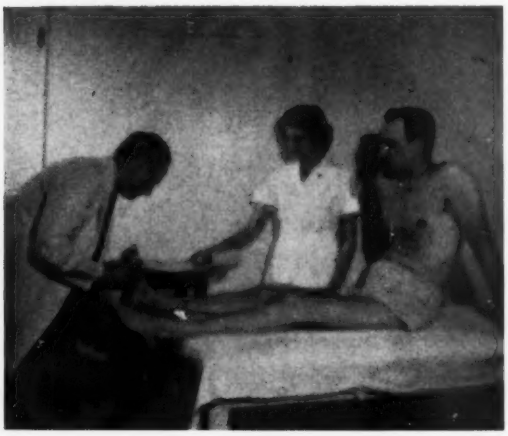
Future Security

Physician must carefully weigh the patient's musculo-skeletal status against the stresses of increased weight, growth, and activity.

Many of our most disabling deformities are caused by persistent faulty skeletal alinement as the patient attempts to resume normal activity. A child with a residual weakness presents a far more difficult problem than does the adult.

The uncontrollable factors of increased bodily weight, asymmetrical bone growth, and the development of substitute patterns of motion to achieve activity combine to cause skeletal distortion.

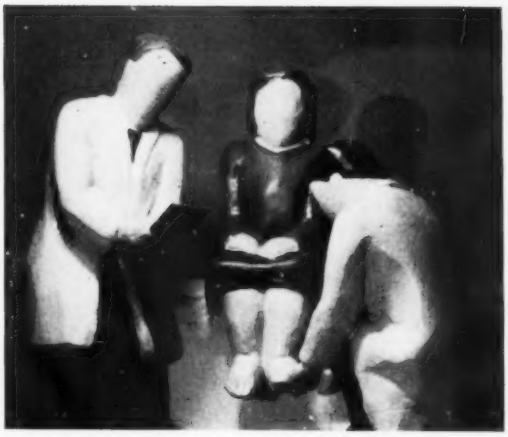
The future security of a bodily segment must never be sacrificed for want of necessary supportive apparatus just to please a patient or his parents, or to make a treatment program "look good" statistically.



Need for Additional Treatment

Plans for future orthopedic surgery to increase functional capacity can be made in the mid-convalescent phase and help determine the necessary interim treatment.

All patients regardless of involvement should be completely evaluated by the physiatrist and orthopedist before dismissal from the hospital. On the basis of this evaluation the present status and probable ultimate involvement should be thoroughly discussed with the patient and/or his family. Instructions in all necessary treatment to be continued at home can be given at this time, as well as definite instructions in type and extent of activity, and time of next medical check-up.



Home Treatment

The responsibility and intelligence of parents in carrying out home routines are all-important in achieving optimum end results.

It is frequently necessary to continue use of supportive and assistive apparatus at school. The teacher must be familiar with the child's treatment program to see that proper use is made of necessary supportive and assistive apparatus.

All patients regardless of involvement will require some form of treatment program continued at home. This program may consist of nothing more than restriction of certain forms of activity in the mild cases. In the more severely involved it might entail close supervision of walking patterns, continued muscle reeducation, correct application of assistive and supportive bracing. The patient and/or his parents must accept the responsibility in order to achieve optimum end results.

Modified Activity

Many activities can be permitted if proper assistive and supportive apparatus is used.

Home routines must be modified to assure continued improvement and/or future security.

Work may be resumed if modified to prevent excessive strain on weakened segments.

Modified activity is an important part of home treatment. Many patients will need nothing more than a partial restriction of normal activity to allow continued improvement.

The moderately involved must modify their activity between periods of muscle reeducation to assure the maximum benefit from these treatments.

Periodic Medical Check-Ups

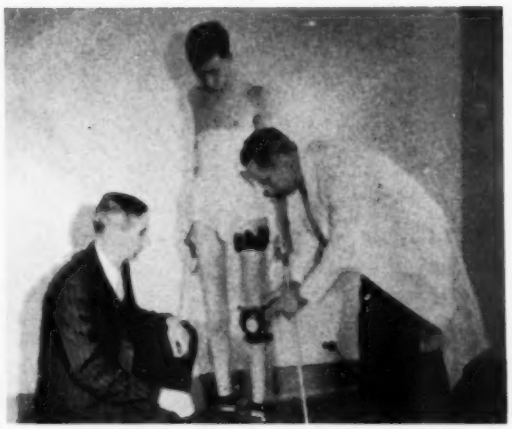
Periodic medical examinations determine the patient's present status, future security, and need for additional treatment.

Repeated muscle tests assist the physician to determine accurately the effect of and necessity for continued home care.

No medical program for the care of the after-effects of poliomyelitis is complete unless it provides for adequate follow-up of its patients.

Maximum return of strength, endurance, and functional activity may require years of guided effort. Many deformities will not occur, nor existing deformities progress until many years after the onset of the disease. Likewise, many supportive, corrective, and assistive orthopedic procedures cannot be carried out with optimum results until patients reach a period of solid bone formation.

The doctor must maintain contact with his patient until maximum functional capacity has been obtained and future security established.



Increase Functional Capacity

Weakness in the abductor brevis and opponens pollicis limits the functional capacity of the entire hand. Transplant of the flexor sublimis tendon of the 4th finger to the thumb may give dramatic improvement.

Peroneal transplant to augment weak dorsiflexors and foot stabilization will permit this patient to walk without a brace.

Even in flail extremities, certain deformities first must be corrected before braces can be applied to permit weight bearing. A light and comfortable brace cannot be fitted around a severe knock knee.

It is frequently possible to increase the functional capacity of the individual patient by orthopedic surgery. In selected cases, the power of a strong muscle of relatively minor importance can be used to increase functional capacity by transplanting its tendon to a new position.

Joint stabilization may allow the removal of cumbersome bracing by limiting the extent of motion in bodily segments unsupported by adequate muscle strength.

Correct Deformity

Correction of musculoskeletal deformities may be necessary before increased functional capacity and future security can be obtained.

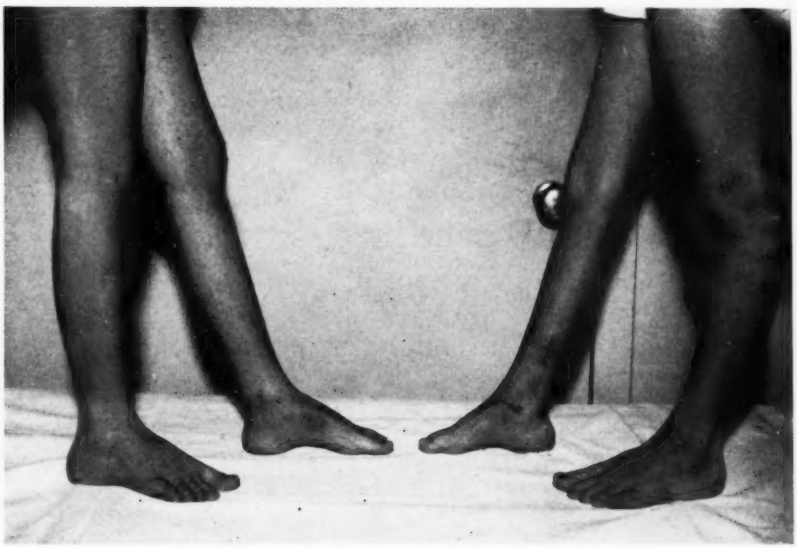
Contractures of the anterolateral hip muscles and iliotibial band not only limit the value of muscle reeducation and gait retraining but also are aggravating factors in progressive scoliosis.

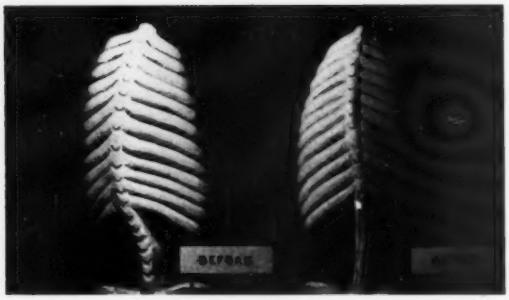
Realinement of skeletal structures may be necessary before maximum use of existing muscle power by tendon transplant is possible or even before light and comfortable braces can be applied.

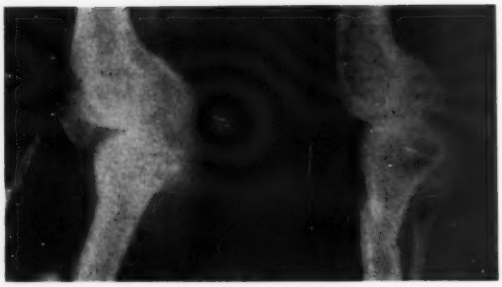
Correction of musculoskeletal deformities and the restoration of functional bodily alinement may be prerequisites for increased functional capacity and future security.

Even when braces must be worn to support weakness, surgery may be necessary to realine bodily segments so that light and comfortable apparatus can be applied.

Certain orthopedic surgical procedures may be necessary early in the convalescent stage before maximum benefit can be obtained from muscle reeducation and gait training. Sectioning of the iliotibial band (see diagram above) should be done as soon as conservative means of stretching fail. This may be within three months after onset. Likewise, sectioning of the tendon achilles may be indicated early and is preferable to forcible wedging if strength in the gastrocnemius-soleus group is fair or better.







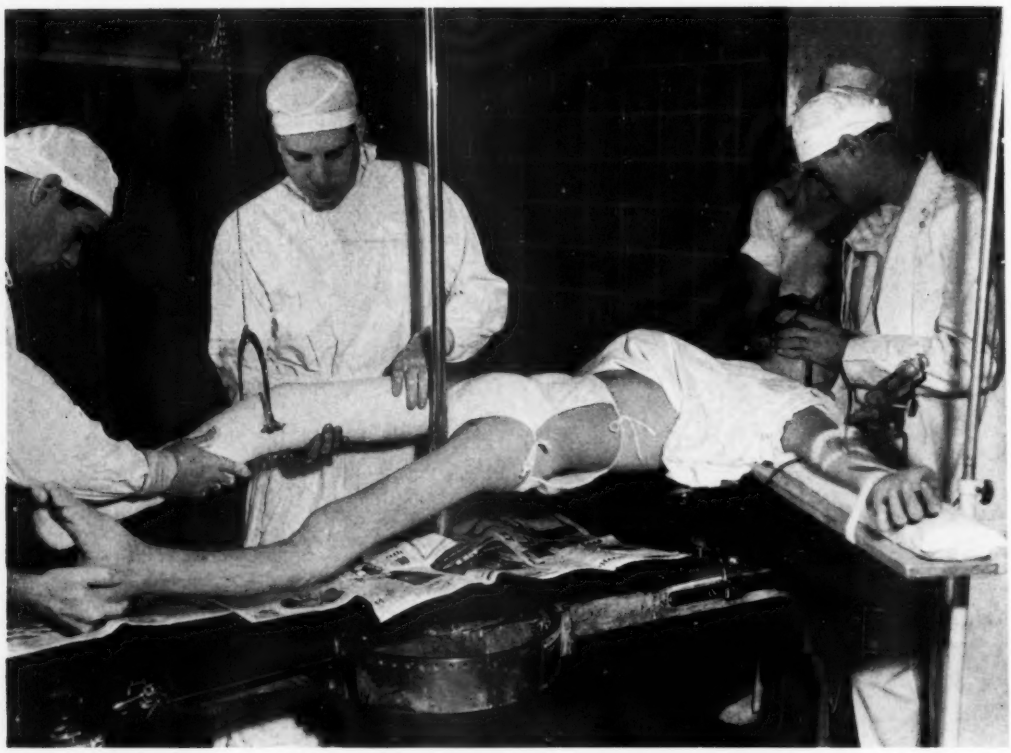
Assure Future Security

The maintenance of good spinal alinement is the most difficult problem in the convalescent and chronic stages of poliomyelitis. Spinal fusion may be necessary to relieve back pain and/or arrest the progression of a scoliosis.

Correct use of plaster casts assures maintenance of skeletal alinement obtained by surgery.

Failure to foresee and prevent faulty weight bearing may result in progressive deformity that can be corrected only by orthopedic surgery.

The continued physical security of the patient is the most serious responsibility of orthopedic surgery. It is absolutely necessary to foresee the effect of growth, increasing weight, age, and activity on weakened bodily segments, and to take adequate precautionary measures when relatively simple surgical procedures will prevent the occurrence of irreversible structural changes. Ideally, surgery should be considered not as a last resort after the damage is done, but rather as a means of preventing these tragedies.



POSTGRADUATE MEDICINE

Preview

Coming issues of POSTGRADUATE MEDICINE *will present these outstanding papers and scientific exhibits, as well as many other valuable and interesting articles, clinics, and special features.*

SPECIAL ARTICLES

The Treatment of Exophthalmic Goiter with Radioiodine—by MAVIS P. KELSEY, Mayo Clinic, Rochester.

Recent Progress in Nutrition—by TOM D. SPIES, Hillman Hospital, Birmingham, Alabama; Professor and Head of the Department of Nutrition and Metabolism, Northwestern University Medical School, Chicago.

The Present Status of Cancer Therapy—by R. LEE CLARK, JR., Director and Surgeon-in-Chief, M.D. Anderson Hospital for Cancer Research, University of Texas, Houston.

DIAGNOSTIC CLINICS

Present Day Rectal Diagnosis—by DOUGLASS PALMER, Assistant Professor of Clinical Medicine, Cornell University Medical College, New York.

Surgical Treatment of Intractable Asthma—by BRIAN B. BLADES, Professor of Surgery, George Washington University School of Medicine, Washington, D.C.

Cancer of the Larynx—by CHEVALIER L. JACKSON, Professor of Laryngology and Bronch-Esophagology, Temple University School of Medicine, Philadelphia.

SCIENTIFIC EXHIBITS

Antibiotic Therapy of Subacute Bacterial Endocarditis—by WALTER S. PRIEST and JACQUES M. SMITH, Wesley Memorial Hospital and Northwestern University, Chicago.

Orthostatic Hypotension and Orthostatic Tachycardia—by ANTON S. YUSKIS and GEORGE C. GRIFFITH, University of Southern California School of Medicine and Los Angeles County General Hospital.

A CONTROVERSIAL CASE

Errors in Electrocardiographic Diagnosis

WILLIAM D. STROUD*

PHILADELPHIA

Although I may be prejudiced since I spent a year with Sir Thomas Lewis in London studying electrocardiography before beginning to interpret tracings in my practice, yet I feel there are entirely too many physicians purchasing galvanometers, taking tracings, and interpreting them without sufficient training in such interpretations. I also feel too many physicians read into electrocardiograms diagnoses which are not justifiable and give the patients the electrocardiograms on which such frightening diagnoses as "myocardial degeneration," etc., have been made.

One of the outstanding internists of Philadelphia has a galvanometer and an associate interprets the electrocardiograms for him.

The manager of an apartment hotel in Philadelphia, age 34 years, discovered a suicide in one of his apartments on January 25, 1947. The individual had been dead for three weeks before he discovered the body. The odor caused him to vomit and then faint. Two days later he developed pain in the left arm and left shoulder blade. He developed a cough and pain across the anterior chest accentuated by deep breathing and ran a low grade fever for several days. The pain had no relation to physical effort.

He consulted the above mentioned internist on January 30, 1947, and electrocardiograms were made, which, as you can see, are entirely normal.

On the chance that he might have had a coronary occlusion, the evidence of which had not as yet developed in the electrocardiograms, he was sent home to bed until February 13, when he returned to the internist's office and the tracings shown were made.

As you can see, the technician reversed the electrodes in Lead I and a mirror image was produced. As a result the internist made a diagnosis of a recent coronary occlusion with myocardial infarction and the patient was sent home to bed for four weeks.

On February 27, 1947, he came to my office. His family history was suspicious as his father at age 56 "has some heart condition" and his mother at age 53 has hypertension. His pulse was 76; blood pressure: right arm systolic 138, diastolic 76; left arm systolic 120, diastolic 76. There was no evidence of cardiac enlargement and no murmurs or abnormalities of the cardiac sounds. The electrocardiograms during the visit were normal.

Through an error in technic and the inability of the internist to recognize a mirror image, this man was invalidized for over a month and it took many weeks to persuade him that he had not had a coronary occlusion.

*Professor of Cardiology, Graduate School of Medicine, University of Pennsylvania, Philadelphia.

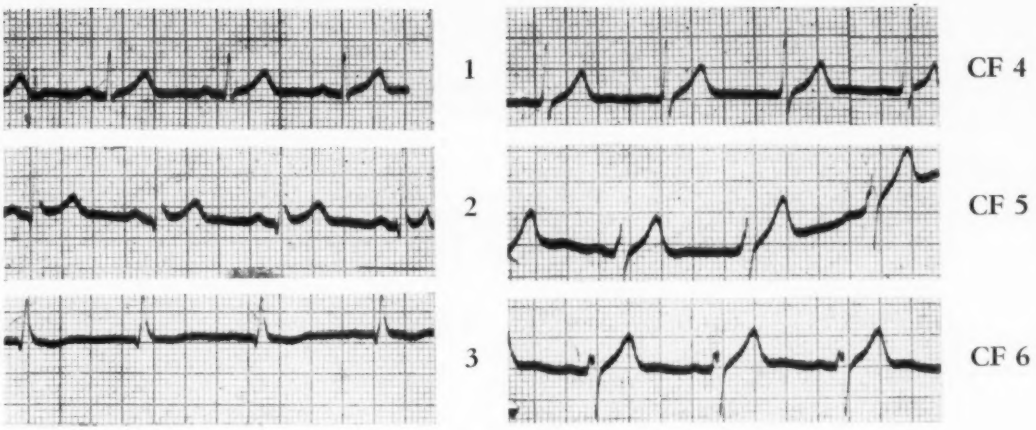


Figure 1. J. B. January 30, 1947

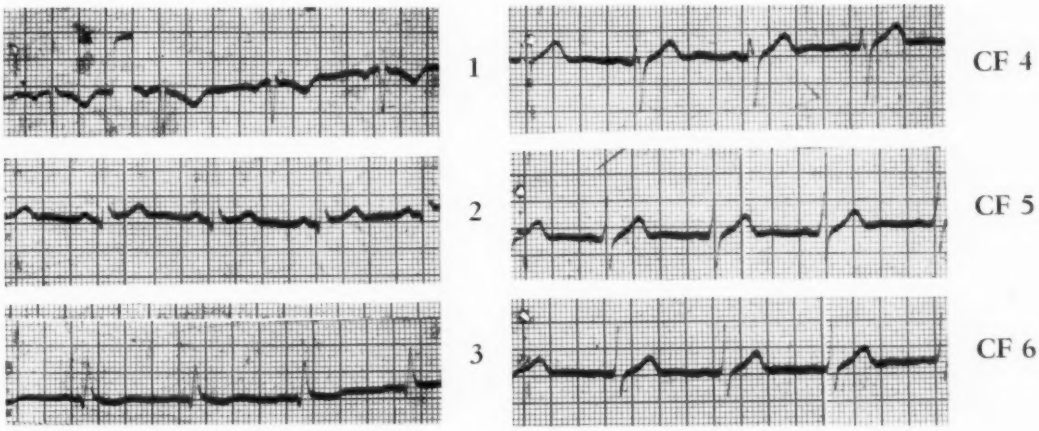


Figure 2. J. B. February 13, 1947

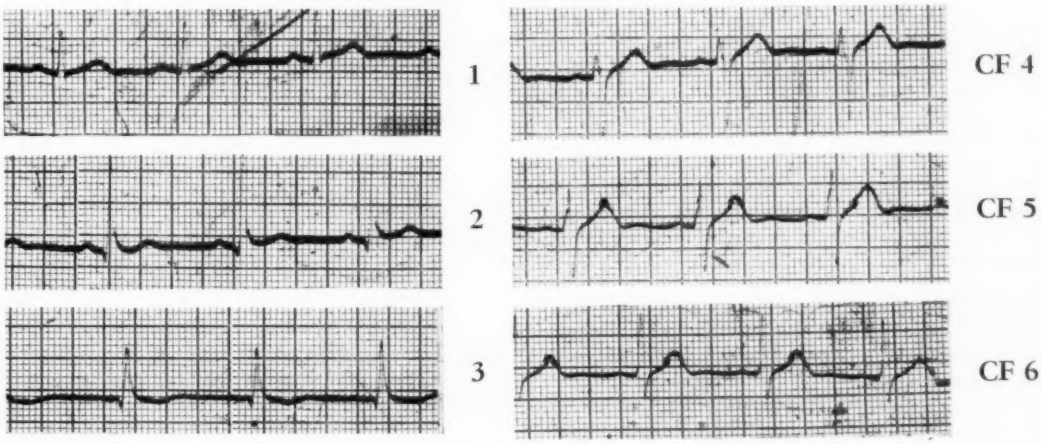


Figure 3. J. B. February 27, 1947

CLINICAL STUDY

Tersavin

A NEW NASAL MEDICATION

ROBERT E. RYAN

ST. LOUIS, MISSOURI

The habitual use of nose drops for a prolonged period of time has been observed to have caused a clinical syndrome designated as "vasomotor rhinitis medicamentosa." This has often been observed grossly in the examination of the nasal passages of persons who have used drops over a long period of time. The histologic effect was also studied and from this it was concluded that the overuse of nose drops was harmful to the nasal mucous membrane.[1]

This does not mean that the use of nose drops for a short period of time, such as during the acute stages of some nasal infection, is contraindicated.

Recently a new product has appeared on the drug market, called Tersavin. It is the crystalline l-ephedrine salt of penicillin G in tablet form. Each tablet contains 30 mg. of the l-ephedrine salt of penicillin G which is equivalent to 30,000 units of penicillin and 9.9 mg. of l-ephedrine. Suitable buffering agents are also added. When one tablet is dissolved in 7.5 cc. of water the solution will be equivalent to ⅛ per cent of l-ephedrine and approximately 40,000 units of penicillin G per cubic centimeter. The *p*H of the solution is said to be 6.0. When the tablets are dissolved in water, the solution will retain its potency at room temperature for about twenty-four hours.

Lierle and Evers report that a penicillin solution containing no less than 5,000 units per cubic centimeter is practically nonirritating when applied directly to the cilia of the nasal mucosa.[2] This solution has about 4,000 units of penicillin G and therefore should not harm the nasal cilia. However, if this solution should be used habitually over a prolonged period of time the effect on the nasal mucosa would probably be as pronounced as that produced with any other form of nasal medication.

In the cases studied in this paper only 7 complained of the solution "burning" or "stinging" when applied to the nasal mucous membrane by dropper method. However, this does not mean that the solution did not produce any severe side effects; in fact 2 of the patients received severe reactions. This was probably due to their sensitivity to penicillin.

These 2 patients both suffered severe skin reactions after using the solution for only twenty-four hours. This reaction was limited to the face and the neck. The nose became very edematous and inflamed both internally and externally. The lips were swollen and a generalized facial discomfort was experienced. These symptoms vanished after the use of the solution had been discontinued for forty-eight hours and antihistamine preparations were administered. These reactions were due to the penicillin in the solution and not to the l-ephedrine as they had both used medication containing ephedrine previously without experiencing any harmful effects. However, neither of the 2 patients had ever been subjected to penicillin in any form before.

Twelve of the patients experienced a little discomfort to the taste of the solution after it had passed from the nasal passages on down into the nasal and oral pharynx. This, however, was a very mild type of side reaction. The side effects noted are shown in Table 1.

TABLE 1

Type of Reaction	No. of Cases
Severe	2
Burning	7
Taste discomfort	12

In all of the cases the vasoconstrictive action of the l-ephedrine was noted by the patient. They all stated that they were able to breathe more freely after the Tersavin had been applied to the nasal mucous membrane. None of the cases in this series received the

medication for a period longer than fourteen days and therefore the use of the drug could not be called habitual or overuse.

Of the cases observed in this report, the majority were of an acute nature. Of the 5 cases of chronic sinusitis observed, not one showed any response to Tersavin after using it for a period of two weeks. No harmful side effects were noted in the 5 patients.

Thirty cases of acute sinusitis were studied. Nine of these patients received some relief from the drug and their symptoms gradually subsided. Eleven of these received only fair results from Tersavin and 10 experienced no relief whatsoever.

Twenty-four patients with acute head colds and a past history of sinusitis following head colds received Tersavin. Of these only 6 developed sinus infections following the head colds. Thirteen of the patients thought that the purulent stage of their head colds was shortened and experienced no sinusitis following the cold. Five patients thought that their colds ran their usual course, but did not experience any attack of sinusitis following the termination of their head cold.

Fifty-three cases of acute coryza were given Tersavin. Thirty of these patients thought that the purulent stage was a great deal shorter than usual. Twenty-three cases found that their acute coryza ran its usual course. The results are tabulated in Table 2.

From these results it seems that this new drug is more effective in acute than in chronic infections. True, the few chronic cases in which it was used do not constitute a fair trial, but because of the definite lack of response, it seemed useless to try it further.

Tersavin seems to be rather effective in the acute infections, especially in reducing the purulent stage of acute coryza. It also seems useful in cases in which there is a history of sinusitis following attacks of acute coryza. Whether the sinusitis would have developed without the use of Tersavin is a question which cannot be answered. However, these patients had a history of experiencing sinusitis following previous attacks of acute coryza.

TABLE 2

Type of Case	No. of Cases	Results		
		Excellent	Fair	Poor
Acute sinusitis	30	9	11	10
Acute coryza	53	30		23
Acute coryza sinusitis	24	13	5	6
Chronic sinusitis	5			5
Total	112	52	16	44

The patient who subjects his nasal passages to overmedication usually does so to relieve a sensation of congestion. The congestion may be due to the normal physiologic activity of the nasal mucous membrane or to certain pathologic conditions of these mucous membranes. The relief afforded becomes less marked as the practice is continued; finally, little or no relief is obtained. The use of nose drops may have been initiated on the patient's own responsibility because of the persuasive effect of advertising by the manufacturers, or in some instances on the advice of physicians who are not thoroughly familiar with the physiology of the nose.

Therefore, since Tersavin does seem to be of some benefit in certain forms of acute nasal pathology, it seems that in order to prevent its habitual or over-use, it should be obtainable only with a physician's prescription. This would greatly prohibit its overuse and prevent the patient from merely going into a drug-store and asking for the preparation of his own accord. If this is done, the manufacturers of Tersavin will have taken a great step in the advancement of nasal medication.

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1. Ryan, Robert E.: Ann. Otol., Rhin. & Laryng. 56:46-57, 1947.

2. Lierle, D. M., and Evers, L. B.: Laryngoscope 54:176, 1944.

The Medical Bookman

CLINICAL ASPECTS AND TREATMENT OF SURGICAL INFECTIONS*

THE subject of surgical infections has usually been written as a single chapter in a textbook of surgery; this is the first publication of a whole book on this subject. Dr. Meleney is well known to the medical world for his many contributions to the literature and more recently for the discovery of bacitracin.

The need for such a book as this has been keenly felt, for now, with the vastly increased armamentarium for the treatment of surgical infections, it has become necessary that the physician become familiar with the specific organism responsible for the disease process in order to properly choose the chemotherapeutic and antibiotic agents. The natural course of the disease and much of what was considered fundamental surgical procedures have been changed with the introduction of these agents.

The book, consisting of 840 pages, is divided into 28 chapters with 287 illustrations, with emphasis placed upon diagnosis and treatment. Case studies are presented in detail to present realistically every phase of the problem. In an all-inclusive text such as this, there is, of necessity, a large number of topics which is not new insofar as there are many common conditions which have formed our knowledge of pathological processes. This, however, seems to make the text even more complete.

In the early part of the book are emphasized certain fundamental concepts—surgical infections should not be considered from a purely bacteriologic standpoint but that chemotherapeutic agents are effective only when they aid the natural defense mechanisms of the body; also, agents effective in normal tissue may be wholly ineffective in abnormal tissue. It is also pointed out that even the strictest aseptic technic must be considered to be accompanied by a certain amount of bacterial organisms with which the so-called "clean wounds" must cope. Particular emphasis is placed on the concept that all forms of treatment should be adopted to supplement the natural defense mechanisms against the bacteria.

Dr. Meleney has had a long standing interest in certain infections of the skin and subcutaneous tissues and the pathogenesis of skin infection—furuncles, carbuncles, cellulitis, and various forms of ulcers—is discussed in detail. Of special interest is the section on "chronic undermining burrowing ulcers." This type of ulcer is not very common but is of interest because of its notorious resistance to treatment. Dr. Meleney has studied various agents and has found that zinc peroxide locally is the therapeutic agent of choice. Sulfonamides have been useful in a small number of cases; penicillin is less effective than sulfonamides. Cases resistant to treatment for many years have been successfully treated by the author's method.

Surgical infections of the head and neck and their mode of spread from the anatomic standpoint are covered in detail. Meleney stresses the need for determining the causative agent before treatment is begun but in instances where treatment must be started at once, cultures should be taken followed by administration of the agent most likely to control infection. Penicillin at present is the drug of choice. However, it is emphasized that many organisms within the staphylococci group are not only resistant to penicillin but also produce penicillinase. Meleney feels that bacitracin must be considered an important substitute for penicillin because of its greater range over nonhemolytic streptococci and because it is not inactivated by penicillinase.

The author feels that if there is no response to drug treatment after forty-eight hours, if the proc-

*Clinical Aspects and Treatment of Surgical Infections, by Frank L. Meleney, M.D., F.A.C.S., Associate Professor of Clinical Surgery, College of Physicians and Surgeons, Columbia University, New York City. 840 pages, illustrated. Philadelphia and London, W. B. Saunders Company, 1949. Price $12.00.

Figure 6. Chronic, undermining, burrowing ulcer of five years' duration. This had already shown some healing under the local application of zinc peroxide but the ulcer burrowed down into the popliteal space between the bone and the hamstring muscle extending from the inner to the outer side of the thigh with a posterior extension into the popliteal space.

Figure 7. Three months later the superficial portion of the wound had entirely healed but the sinus through the leg had persisted owing to the inability to obtain proper contact with the medicine. *(Illustrations from: Meleney, "Clinical Aspects and Treatment of Surgical Infections.")*

ess progresses in spite of drug therapy, or if improvement comes to a standstill, surgical treatment is recommended but should be delayed until some evidence of localization of the process is present. He states that in general there is a tendency to wait longer before surgical procedures are carried out in this region because of unpleasantness of resulting scars.

In treatment of actinomycosis the author feels that if all gross evidence of disease can be removed surgically, it should be done and penicillin and bacitracin given to prevent reactivation of residual organisms that contaminate the operative field. Reference is made to others who feel that intensive penicillin therapy is the treatment of choice.

Twenty-five pages are devoted to discussion of surgical infections of the heart, pericardium, and mediastinum. The great majority of mediastinitis follows the entrance of organisms into this region from perforation of the esophagus. The author quotes the studies of Adams who has had extensive experience with acute suppurative mediastinitis, and who states that a favorable outcome depends largely upon:

(a) Prompt extrapleural mediastinotomy, (b) gastrostomy, and (c) massive chemotherapy.

In subacute bacterial endocarditis penicillin is stated to be the treatment of choice. Most in-

Figure 8. After several tries, the infection was brought under control by enlarging the opening so as to permit more intimate contact with the zinc peroxide. The wound is ready for skin-grafting, both in the tunnel and in the posterior extension.

Figure 9. Seventeen days later the wound had completely healed.

vestigators advocate as much as 1,000,000 units of penicillin daily for as long as eight to ten weeks. Although surgery has not been attempted, Meleney feels that it is not improbable that some procedure will be developed to remove vegetations. In suppurative pericarditis chemotherapy plus dependent drainage or chemotherapy plus needle aspirations is recommended.

Every page of the chapter on management of infections of the lungs and pleura contains valuable information. There are numerous illustrations and x-ray reproductions and detailed accounts of such conditions as bronchiectasis, lung abscess, and gangrene of the lungs. This chapter is especially important in view of the rapid progress being made in thoracic surgery.

Infections of the peritoneum are covered separately and in detail. In summing up the treatment the author states that the most important factor is that of prevention since peritonitis is usually a complication of some other condition. When the diagnosis of peritonitis is established, the principles of treatment are summarized as follows:

(a) Treat focus preferably by removing it or otherwise by draining it. (b) Treat the complications, chiefly ileus. (c) Combat toxins and bacteria directly. (d) Drain all abscesses.

Meleney feels that a combination of sulfadiazine, streptomycin, and penicillin is probably the best to administer. Regarding drainage he states that there are certain well established facts which must be kept in mind. The first is that any drain placed in

the peritoneal cavity excites an inflammatory response so that it becomes walled off within a few hours except where there is profuse drainage. Drains should be placed to reach the skin by the shortest possible route, and the tissues should not be sewed too closely about the drain.

The sections on liver, spleen, pancreas, and biliary tree are presented in detail with many illustrative case histories and particular emphasis upon treatment. The entire gastrointestinal tract and genitourinary tract is treated in like manner.

Of especial interest is the chapter on appendicitis which includes a very interesting historical review of progress in knowledge of the recognition of the disease, diagnosis, and treatment. As to causation of appendicitis three main possibilities are given: (a) enterogenous, (b) hematogenous, and (c) intrinsic. Evidence is presented to suggest that the first two categories are rather unlikely.

The author has found that 80 per cent of all cases of appendicitis are on an obstructive basis and of these 67 per cent were caused by impacted fecaliths. With obstruction the intraluminal pressure is built up not only by the inflammatory exudation but also by the mucoid secretion of the appendix and by gas from pus forming organisms. As distension increases the blood supply of the wall diminishes and as the bacteria invade the appendiceal wall, thromboses of vessels take place. This further favors growth of bacteria even of a low grade pathogenicity.

Considerable discussion is offered on the bacteriology of appendicitis. It is assumed that before an attack of appendicitis begins or before the lumen becomes occluded, all the intestinal species found in the cecum are also present in the appendix. The author states that it is difficult to be sure whether such organisms have the power of initiating inflammation of the appendix because when an inflamed appendix is removed, there is almost always evidence of pressure by the contained fecal material.

With perforation the contents of the appendix are discharged into the peritoneal cavity and if the proximal appendix is not blocked, fecal material from the cecum pours into the peritoneal cavity. One cannot thus be sure that the organisms cultured from the peritoneal cavity or from the lumen of the appendix when the appendix has perforated have taken any real part in the production of the inflammation. Dr. Meleney has found that there is real significance in the observation that cultures of the peritoneal surfaces of gangrenous appendices without perforation frequently reveal organisms of the E. coli group. Apparently they are able to penetrate the compromised appendiceal wall.

A correlation was established between the bacteriology of peritoneal exudates and the clinical course of 106 cases of peritonitis. Of these, 76 were due to lesions of the appendix. In 37 there was acute appendicitis without perforation; in 30 the appendix had perforated and in 9 there was gangrene of the appendix without perforation. Of the 37 cases of acute appendicitis without gangrene or perforation, 7 demonstrated that it is possible for bacteria to penetrate a grossly intact appendiceal wall. E. coli was apparently more likely to do this than any other organism. The Welch bacilli and green streptococci were able to do it in association with E. coli but never alone.

The author ascribes the cause of gangrene of the appendix to the factor of occlusion of blood vessels or of pressure necrosis to be of major importance before liquefaction of tissue and perforation can take place. Signs and symptoms are essentially those commonly given.

Reference is made to the work of others who had found auscultation of the abdomen of value. In 444 cases of diffuse peritonitis of appendiceal origin, those in whom auscultation failed to reveal peristalsis had a mortality rate three times higher than those in whom peristalsis could be heard. Considerable discourse is given on variation in signs and symptoms. The white blood cell count is often misleading; it is usually moderately elevated, averaging around 16,000 to 18,000 with 80 to 82 per cent polymorphonuclear cells. The writer emphasizes that this should not be the criterion on which to base the necessity for operation, for a gangrenous appendix is not infrequently present with no rise in white cell count.

Meleney states that the proper treatment of all cases of appendicitis is surgical removal within twenty-four hours after onset. A lengthy discussion is given on Ochsner's method of conservative treatment of appendicitis delayed for more than twenty-four to forty-eight hours. He feels that the greatest danger of this conservative treatment is the encouragement it gives to general practitioners to apply it to all cases of appendicitis no matter

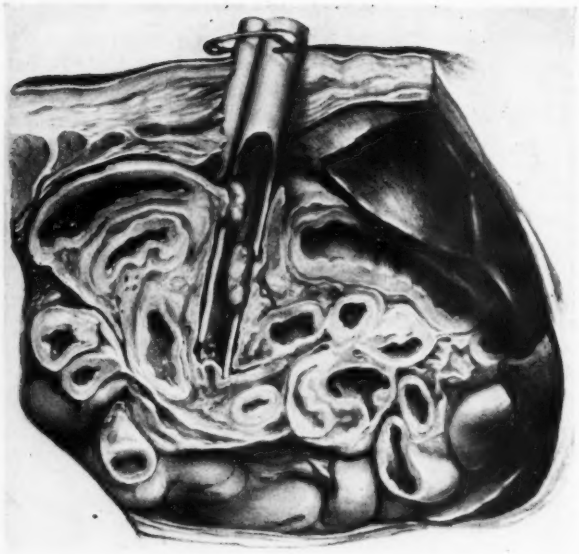


Figure 114. Drawing of peritoneal drainage in a dog, illustrating why peritoneal drains are effective over such a small area. Under ether anesthesia, gangrene of the cecal appendage was caused in a dog by ligating the vessels leading to it and tying off the base of the appendate. A double-tube drain was placed down into the site and left in place for two weeks, after which time the animal was sacrificed. The drawing shows the tube in place with viscera closely adherent everywhere about it. Fenestra, which had been cut in the tube, are plugged by buds of granulation tissue. The drain is effective nowhere more than a centimeter from its bed. Had it not been placed accurately and maintained in place, it could have failed wholly of its purpose.

how early they are seen. It is emphasized that Ochsner strongly favored appendectomy for patients seen within twenty-four to forty-eight hours after onset and furthermore he always advised appendectomy after the attack was over in conservatively treated patients.

The author presents many references citing certain advantages of chemotherapeutic and antibiotic agents, but in his final analysis he states that these agents are of secondary importance. Stress is placed upon early diagnosis and prompt removal of the appendix. In his own method of treatment Dr. Meleney does not give drugs to patients with acute nonperforated appendicitis operated upon within the first forty-eight hours after onset unless complications develop later. In cases in which perforation has taken place sulfadiazine is given in an initial dose of 4 gm. followed by 1 gm. every four hours. Penicillin is given in a dosage of 100,000 units every three hours and streptomycin in a dosage of 0.5 gm. every three hours. The streptomycin is stopped after four days; penicillin is stopped after six or seven days, and the sulfadiazine after eight to ten days. This program is modified to some extent to meet the needs of each case. The fluid and electrolyte balance is maintained and decompression of the bowel is maintained by suction from above. Fifteen case histories are presented in detail to show the various problems involved in this disease.

Every phase of the problem of bone and joint and infection of the hand is dealt with. A completely separate chapter is devoted to infections of the central nervous system and to surgical septicemia, and the book concludes with a chapter on war wounds. This section contains much that is not available in other present day texts.

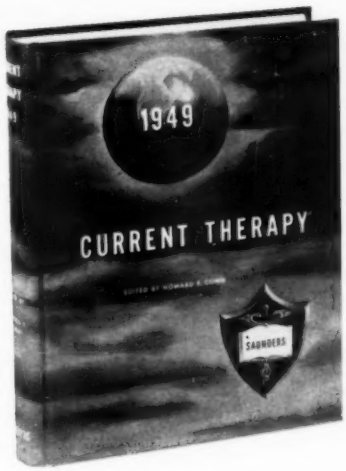
In all subjects covered the discussion is amplified by a good cross section of opinion of other investigators interested in the problem. An excellent bibliography accompanies each chapter. This book points out rather strikingly that a good surgeon must not lose contact with the first hand information which can be made available by having an active bacteriologic laboratory connected with every surgical service. Because of the systematic presentation and illustrative cases accompanying each subject, the reader will find this text to be a veritable gold mine in understanding the pathogenesis, diagnosis, treatment, and prognosis of surgical infections.

Y. S.

New Books Received

► CURRENT THERAPY 1949—Latest Approved Methods of Treatment for the Practicing Physician - - -

By Howard F. Conn, M.D., Editor. Consulting Editors: M. Edward Davis, Vincent J. Derbes, Garfield G. Duncan, Hugh J. Jewett, William J. Kerr, Perrin H. Long, H. Houston Merritt, Paul A. O'Leary, Walter L. Palmer, Hobart A. Reimann, Cyrus C. Sturgis, Robert H. Williams. 672 pages. Philadelphia and London, W. B. Saunders Company, 1949. Price $10.00.



Recognizing the need for concise, authoritative information on treatment of a multitude of diseases, the editors of this book have assembled original discussions by eminent practitioners in nearly every specialty. Starting with the assumption that in every instance the diagnosis has already been established, each contributor presents his method of treating the disease in question. Where there are varying opinions on the treatment of a certain disease, the methods of two or more authorities are offered without any claims as to their relative merits.

The book is arranged in sections according to classification of diseases—as, for example, the Infectious Diseases, Diseases of the Digestive System, etc. In addition to a general listing of contents, each section is preceded by a list of diseases discussed therein and the whole book is thoroughly indexed.

S. C.

► FUNDAMENTALS OF TUBERCULOSIS AND ITS COMPLICATIONS - - -

Edited by Edward W. Hayes, M.D. (Sponsored by the American College of Chest Physicians). 480 pages. 1949, Charles C Thomas, Springfield, Illinois. Price $9.50.

Tuberculosis is still one of the most formidable public health problems in the world. Being acutely aware of this fact, the American College of Chest Physicians, under the editorship of Dr. E. W. Hayes, have prepared this illustrated text bringing together the opinions of 27 leading authorities in this field. This text is not meant to cover all the aspects as in a large treatise on this subject but to give more than that which is found in a standard textbook of medicine.

The first few sections deal with the anatomy, bacteriology, and the pathologic picture of tuberculosis. These sections are well illustrated with photographs, x-ray reproductions, and with photomicrographs, some in color. In subsequent chapters particular emphasis is placed on differential diagnosis of reinfection types of tuberculosis. Twenty-two of the major chest diseases are considered in detail under differential diagnosis. This section is worthy of careful scrutiny by all students and practitioners.

Over 120 pages are devoted to the treatment of tuberculosis, including the latest opinion regarding antibacterial treatment. The chapter on surgical procedures gives indications and types of surgical procedures available with detailed discussions and case histories of end results obtainable.

Special consideration is given to psychosomatic aspects of tuberculosis, pregnancy, diabetes, and silicosis and its relationship to pulmonary tuberculosis. An entire chapter is also devoted to the public health aspects of tuberculosis. Considered separately under complications are tuberculosis of the larynx, tuberculous enterocolitis, and tuberculosis of the urinary tract. Twenty other complications are discussed in still another chapter.

This text is written not for a physician interested in tuberculosis only, but for all men who practice medicine; to emphasize in a few brief chapters the highlights of our present knowledge of this disease so that no matter what branch of medicine one practices, he will be able to make a diagnosis of tuberculosis should he be the first to see the patient.

Y. S.

► THE CHEST AND THE HEART - - -

Section I, The Chest, Edited by J. Arthur Myers, Ph.D., M.D., Professor of Medicine and Preventive Medicine and Public Health, University of Minnesota Medical and Graduate Schools; Section II, The Heart, Edited by C. A. McKinlay, M.D., Clinical Associate Professor of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota. In two volumes of 1800 pages with 769 figures showing 1003 illustrations. 1948, Charles C Thomas, Springfield, Illinois. Price $25.50.

With the aid of 59 collaborators, Dr. Myers and Dr. McKinlay have edited this comprehensive review of diseases affecting the lungs, the heart, and contiguous structures. Fundamental discussions of anatomy, physiology, and pathology lay the groundwork for the clinical approach to the disease entities which are covered in most complete fashion. Methods of special examinations are explained in detail and will be extremely valuable to the practicing physician. This completeness has produced a work which will serve the general practitioner as well as the specialist, the teacher as well as the student.

The inclusion of all diseases of the chest in the two volumes is logical since there is often a close association between pulmonary and cardiac diseases. Each chapter is summarized and the contents are well indexed. The printing and illustrations are excellent.

S. S. C.

► CARDIOLOGY - - -

By William Evans, M.D., D.Sc., F.R.C.P. 310 pages, illustrated. Paul B. Hoeber, Inc., New York, 1948. Price $7.50.

This book, by an eminent English author, is a concise treatise on the subject of heart disease. The initiative for this work was a series of lectures given to postgraduate students at the London Hospital.

Methods of examination, diagnosis, and treatment are fully discussed. The book is profusely illustrated with x-rays, electrocardiograms, phonocardiograms, and diagrams depicting various conditions. These illustrations are uniformly good.

The chapter on heart murmurs and their interpretation is a clear and lucid presentation of this subject.

The chapter on electrocardiography does not mention the use of unipolar and augmented extremity leads. This should have been included.

It is refreshing, however, to get the viewpoint of our confreres across the sea on the management of heart disease, and the work should prove of interest to the busy practitioner who wants to brush up on his cardiology.

T. L.

► HAVING YOUR BABY - - -

By Leonard H. Biskind, M.D., Acting Director, Department of Obstetrics and Gynecology, Mount Sinai Hospital, Cleveland. 96 pages. Western Journal of Surgery Publishing Company, Portland, Oregon, 1949. Price $2.50.

The author has designed this booklet with the purpose of offering sufficient practical information about pregnancy, labor, and delivery to alleviate anxiety in expectant mothers. The text is well organized in easily readable outline form and is adequately indexed. A glossary of medical and obstetrical terms should be valuable to lay readers.

In books of this type a definite line should be drawn beyond which specialized information that is of no value to the patient is omitted. In general the author has accomplished this restriction admirably, but with a few exceptions. For example, the fact that breech presentation is of more concern in the primipara may be alarming to the patient. The concern should be the obstetrician's The reader is told that most deliveries are now performed by means of prophylactic forceps and that the use of vitamin B complex during pregnancy permits the patient to get out of bed sooner with less danger of bleeding. The patient should not be asked to accept information that may be controversial to physicians.

Despite the above, the booklet should prove a valuable contribution to the curious or anxious prenatal patient and to her busy but usually critical doctor. M. B. S.

Books received will be acknowledged in this department each month. As space permits, books of principal interest to our readers will be reviewed more extensively.

NEURORADIOLOGY. By Alexander Orley, M.D., F.F.R., D.M.R. & E., Hon. Consulting Radiologist, West End Hospital for Nervous Diseases, London. 436 pages, 572 illustrations. 1949, Charles C Thomas, Springfield, Illinois. $11.50.

THE TEMPORAL BONE AND THE EAR. By Barry J. Anson, M.D., Professor of Anatomy, Northwestern University Medical School, and Theodore H. Bast, M.D., Professor of Anatomy, University of Wisconsin. 498 pages. 1949, Charles C Thomas, Springfield, Illinois. $12.00.

DISEASES OF THE LIVER, GALLBLADDER AND BILE DUCTS. By S. S. Lichtman, M.D., F.A.C.P., Assistant Professor of Clinical Medicine, Cornell University Medical College, New York. Ed. 2. 1135 pages, 147 illustrations with 4 in color. 1949, Lea & Febiger, Philadelphia. $18.00.

A PRIMER OF ELECTROCARDIOGRAPHY. By George E. Burch, M.D., F.A.C.P., Henderson Professor of Medicine, Tulane University School of Medicine, New Orleans; and Travis Winsor, M.D., F.A.C.P., Assistant Clinical Professor of Medicine, University of Southern California Medical School, Los Angeles. Ed. 2. 245 pages, 265 illustrations. 1949, Lea & Febiger, Philadelphia. $4.50.

CHILD PSYCHIATRY. By Leo Kanner, M.D., Associate Professor of Psychiatry, the Johns Hopkins University, Baltimore. Ed. 2. 752 pages. 1948, Charles C Thomas, Springfield, Illinois. $8.50.

MAYO CLINIC DIET MANUAL. By the Committee on Dietetics of the Mayo Clinic. 329 pages. 1949, W. B. Saunders Company, Philadelphia & London. $4.00.

OBSTETRIC ANALGESIA AND ANESTHESIA. By Franklin F. Snyder, M.D., Associate Professor of Obstetrics and Associate Professor of Anatomy, Harvard Medical School. 401 pages, 114 figures and 18 tables. 1949, W. B. Saunders Company, Philadelphia & London. $6.50.

OBESITY. By Edward H. Rynearson, M.D., F.A.C.P., Division of Medicine, Mayo Clinic; Associate Professor of Medicine, Mayo Foundation, and Clifford F. Gastineau, M.D., Fellow in Medicine, Mayo Foundation, Rochester, Minnesota. 144 pages, 9 figures, 16 tables. 1949, Charles C Thomas, Springfield, Illinois. $3.50.

AN ATLAS OF ELECTROCARDIOGRAPHY. By William Dressler, M.D., Cardiologist, Maimonides Hospital, Brooklyn; Consultant in Cardiology, The Brooklyn Hospital; Lecturer in Medicine, Long Island College of Medicine, and Hugo Roesler, M.D., Cardiologist, Department of Medicine; Associate Professor of Radiology, Temple University Medical School and Hospital, Philadelphia. 503 pages, illustrated. 1949, Charles C Thomas, Springfield, Illinois. $14.00.

CARDIAC CATHETERIZATION IN CONGENITAL HEART DISEASE. By André Cournand, M.D., Associate Professor, Department of Medicine, College of Physicians and Surgeons, Columbia University; Janet S. Baldwin, M.D., Assistant Professor, Department of Pediatrics, New York University College of Medicine; and Aaron Himmelstein, M.D., Instructor, Department of Surgery, College of Physicians and Surgeons, Columbia University. 108 pages, illustrated. 1949, The Commonwealth Fund, New York. $4.00.

POSTTRAUMATIC EPILEPSY. By A. Earl Walker, M.D., Formerly Professor of Neurologic Surgery, University of Chicago; Now Professor of Neurologic Surgery, Johns Hopkins University, Baltimore. 86 pages. 1949, Charles C Thomas, Springfield, Illinois. $2.75.

MEDICINE THROUGHOUT ANTIQUITY. By Benjamin Lee Gordon, M.D., Member American Association of the History of Medicine and American Academy of Ophthalmology and Otolaryngology; Author of The Romance of Medicine. 840 pages, 157 illustrations. 1949, F. A. Davis Company, Philadelphia. $6.00.

THE ADRENAL GLAND. By Frank A. Hartman, Ph.D., Research Professor of Physiology, Ohio State University, and Katharine A. Brownell, Ph.D., Instructor in Physiology, Ohio State University, Columbus, Ohio. 581 pages, 72 illustrations. 1949, Lea & Febiger, Philadelphia. $12.00.

PAIN SYNDROMES; TREATMENT BY PARAVERTEBRAL NERVE BLOCK. By Bernard Judovich, M.D., Instructor in Neurology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, and William Bates, M.D., F.A.C.S., F.I.C.S., Professor of Surgery, Graduate School of Medicine, University of Pennsylvania. Ed. 3. 374 pages, 181 illustrations. 1949, F. A. Davis Company, Philadelphia. $6.00.

PRACTICAL ASPECTS OF THYROID DISEASE. By George Crile, Jr., M.D., F.A.C.S., Department of Surgery, Cleveland Clinic. 355 pages with 101 figures. 1949, W. B. Saunders Company, Philadelphia & London. $6.00.

BLOOD TRANSFUSION. By Elmer L. DeGowin, M.D., Associate Professor of Internal Medicine, State University of Iowa; Robert C. Hardin, M.D., Assistant Professor of Internal Medicine, State University of Iowa; and John B. Alsever, M.D., Senior Surgeon, U. S. Public Health Service. 587 pages with 200 diagrammatic drawings. 1949, W. B. Saunders Company, Philadelphia & London. $9.00.

SURGERY OF THE HAND. By Sterling Bunnell, M.D., Honorary Member of the American Academy of Orthopedic Surgeons, Consultant in Hand Surgery to the Surgeon General. Ed. 2. 930 pages, illustrated. 1949, J. B. Lippincott Company, Philadelphia. $16.00.

PSYCHIATRY FOR THE PEDIATRICIAN. By Hale F. Shirley, M.D., Associate Professor of Pediatrics and Psychiatry, Stanford University School of Medicine, San Francisco. 442 pages. 1948, The Commonwealth Fund, New York. $4.50.

DISCOVERERS FOR MEDICINE. By William H. Woglom, M.D. 229 pages, illustrated. 1949, Yale University Press, New Haven, Connecticut. $3.75.

HOW TO BECOME A DOCTOR. By George R. Moon, A.B., M.A., Examiner and Recorder, University of Illinois Colleges of Medicine, Dentistry and Pharmacy. 131 pages. 1949, The Blakiston Company, Philadelphia and Toronto. $2.00.

FUNDAMENTALS OF INTERNAL MEDICINE. By Wallace Mason Yater, A.B., M.D., M.S. (in Med.), F.A.C.P., Director, Yater Clinic, Washington, D. C.; Formerly Professor of Medicine and Director of the Department of Medicine, Georgetown University School of Medicine, Washington, D. C. Ed. 3. 1451 pages, 315 figures. 1949, Appleton-Century-Crofts, Inc., New York. $12.00.

ALLERGY; WHAT IT IS AND WHAT TO DO ABOUT IT. By Harry Swartz, M.D., Clinical Assistant, Allergy Out Patient Department, Roosevelt Hospital, New York. 210 pages. 1949, Rutgers University Press, New Brunswick, New Jersey. $2.75.

PATHOLOGY AND SURGERY OF THYROID DISEASE. By Joseph L. DeCourcy, M.D., Senior Surgeon, Good Samaritan Hospital; Director, DeCourcy Clinic, and Cornelius B. DeCourcy, M.D., Member, DeCourcy Clinic Surgical Staff, Cincinnati, Ohio. 476 pages, illustrated. 1949, Charles C Thomas, Springfield, Illinois. $10.00.

EDITORIALS

REPORT ON VETERANS ADMINISTRATION MEDICAL SERVICE

THE 129 hospitals and the corollary medical services of Veterans Administration are a vast proving ground where it is being demonstrated for the first time in the history of the Nation that Government and Medicine can work together on a voluntary and cooperative basis as a highly effective team to provide patients with care and treatment that are recognized as being unsurpassed.

This successful experiment in cooperative medicine has attracted such wide attention that many foreign governments have sent representatives to the United States to study its operation.

American medical journals have appraised the program as a milestone in the history of Medicine—a milestone of progress in applying new principles to the common effort of Government and Medicine toward giving patients the best type of care and treatment.

This working agreement did not just happen. It was carefully worked out to assure a medical service freed as nearly as possible of regulatory restrictions, but which could work with other VA departments so as to improve all service to veterans.

The program was initiated shortly after General Omar N. Bradley became Administrator of Veterans Affairs late in 1945. It was part of an overall plan to vitalize and streamline a Federal agency that was expected to provide the greatly increased benefits which a grateful people had enacted into law through their Congress for approximately 18,000,000 veterans of all wars and their dependents.

General Bradley appointed Major General Paul R. Hawley as his chief medical director to reorganize VA's Medical Service in line with this general plan of operation.

Generals Bradley and Hawley conferred at length with scores of outstanding medical leaders throughout the country, including Dr. Paul B. Magnuson, whom I later named Chief Medical Director. Many of these medical leaders were so enthusiastic over the possibilities of a great cooperative effort between Medicine and Government that they joined the team drafting the program.

The plan of operation that they evolved became the official VA program in January of 1946 with the passage of the law establishing the VA's present Department of Medicine and Surgery.

The law enabled VA to enlist the services of the Deans of our great medical schools and other outstanding men in the profession to set standards and qualifications that would achieve the country's objective of providing medical care for eligible veterans second to none.

The law further provided for the appointment of a Medical Advisory Council, composed of recognized authorities in the medical profession, to serve as advisors to the Administrator on medical and surgical questions.

Under this broad setup, VA's hospitals became affiliated with most of the great teaching schools of the country to establish a teaching program in VA hospitals under outstanding consultants. In that manner, VA made the practice of medicine in its hospitals and medical services highly attractive to the profession.

Since VA is an integrated agency administer-

ing a wide variety of benefits other than medical care, General Bradley had to provide these services in VA hospitals and integrate them into the overall administrative program.

Let us examine some of the problems involved in this broad administrative program. The adjudication of claims for disability compensation or pension combines medical findings with legal requirements; hence, our doctors are only a part of the team that handles this benefit. The actual administrative processes, however, have scarcely anything to do with the practice of medicine. For that reason, they are assigned to highly trained specialists in adjudication.

The administration of our insurance program frequently requires the services of doctors for the physical examinations that must accompany applications for insurance and for granting premium waivers for disability; yet, the administrative machinery for insurance has little or nothing to do with the practice of medicine.

Conversely, our Department of Medicine and Surgery needs the services of other departments to function properly; namely, Finance, Supply, Construction, Maintenance and so on. These departments, in turn, provide service for divisions of VA other than the Department of Medicine and Surgery.

By combining these departments and divisions into an administrative whole, the Administrator is able to fulfill his functions and responsibilities under the various laws he is required to administer.

Many of these non-medical services are represented in our hospitals; but, because of their non-medical functions and responsibilities, the personnel in these services are, of necessity, responsible to other Assistant Administrators and, through them, to the Administrator of Veterans Affairs, just as the medical personnel in the Department of Medicine and Surgery are responsible to the Chief Medical Director and, through him, to the Administrator.

That is the type of organization General Bradley set up to fulfill his responsibilities as Administrator under the diverse laws enacted by the people of the United States through their Congress. And that is the organization I inherited when I succeeded General Bradley as Administrator of Veterans Affairs.

Today, except for the elimination of the former Branch Offices and their secondary supervisory functions, the organization remains exactly as it was set up by General Bradley.

This, then, is the type of organization that has achieved such remarkable results in improving the care and treatment of patients through the voluntary cooperation of both Government and Medicine.

And since this pioneering effort is contributing such a distinguished chapter to the history of both Government and Medicine, it is essential that we continue our cooperation to the end that we may further improve the already high quality of medical care we now give.

In the light of that desire, I am happy to have this opportunity to thank the medical profession for its great contribution to our progress thus far and to express the wish that Medicine will continue its contribution to our further success in the future.

CARL R. GRAY, JR.
Administrator of Veterans Affairs,
Veterans Administration

TELEPHONING NARCOTIC PRESCRIPTIONS

IN A published warning to druggists, H. J. Anslinger* cautions them against filling prescriptions for narcotic drugs in response to telephoned orders. The point is clearly made, however, that, while the law applies equally to the physician and the druggist, *the primary responsibility rests with the physician.*

Although they can and should refuse to fill telephoned orders for narcotic drugs, many druggists continue to fill such requests in a desire to accommodate their physician customers. The fact that in most instances the physician has no intention of violating the law or implicating the druggist in a violation does not lessen

*U. S. Commissioner of Narcotics.

the offense. In fact, it only makes it easier for a deliberate offender to secure narcotic drugs and also tends to make the druggist less wary of telephoned orders from addicts or suppliers of addicts who represent themselves as physicians.

The indiscriminate telephoning of such orders has resulted in a real problem of diversion of narcotic drugs to addicts. Rather than risk antagonizing a physician, druggists have accepted telephoned orders to deliver narcotic drugs to patients who are actually addicts and who have pretended to be physicians over the phone for the purpose of obtaining supplies of drugs to satisfy their addiction.

For their own protection and that of the druggist and to comply with the definite provisions of the Federal Narcotic Law and the Uniform State Narcotic Act, the physician should not only avoid telephoning orders for narcotic drug prescriptions, but should also be sure to execute such prescriptions properly.

In order to be sure that he is not an accessory to violations of the Narcotic Law, the physician should observe the following precautions:

1. Write and sign all prescriptions for narcotic drugs.

2. Date and sign all prescriptions for narcotic drugs on the date issued and include full name and address of patient and name, address and registry number of the practitioner. Prescriptions should be typed or written with ink or indelible pencil; if typewritten, they should be signed by the doctor.

3. Issue prescriptions for narcotic drugs for legitimate medical purposes only; do not issue orders to provide an addict or habitual user of narcotics with drugs for his use.

4. Do not use a prescription form to obtain narcotic drugs for general office practice. Official order forms are available for this purpose from a qualified manufacturer or wholesale dealer.

5. If a genuine emergency exists, the physician may telephone an order for narcotic drugs but should always supply the druggist with a properly executed prescription at the time the delivery is made.

A. E.

CARDIAC NEUROSIS

Although cardiac neurosis may be defined as a nonstructural defect composed of a symptom complex involving anxiety concerning the heart and blood vessels, it is, of course, necessary to eliminate the presence of an actual organic defect before establishing the diagnosis. In a discussion of the subject, Dr. Gilbert H. Marquardt listed three factors which are usually present in patients developing cardiac neuroses: (1) an anxiety cycle; (2) tendency to hysterical reactions; (3) conversion hysteria to a cardiac symptom.

It was found during the war that the usual age group affected was that suitable for military service, and especially combat duty, but the symptoms may arise in patients of any age group. While it is probably true that a history of so-called family neuroses could be discovered in many cases, this "predisposition" is too broad a category to warrant generalization. However, there is usually evidence of the presence of hyperanxiety and other similar precipitating factors.

The symptomatology of the condition includes pain, varying from a dull ache to a sharp but fleeting sensation, which bears no relation to physical exertion; tenderness, fainting, and simple tachycardia. The physician must evaluate the symptoms carefully, paying special attention to signs of palpitation, consciousness of the heart's beating, and arrhythmia; dyspnea and sighing respiration; sweating, dizziness, and acidosis.

Tenderness is usually superficial, but there is apparently a real hyperalgesia. Weakness and fatigability are marked, and fainting is apt to occur. If there are tremors, they tend to be of the moderately coarse type. The symptoms almost fall into a pattern and no special significance should be attached to them.

As stated earlier, the heart must be examined carefully to be sure that there is no structural heart defect. If heart function appears to be normal, it is possible to arrive at the diagnosis by a process of exclusion. Dr. Marquardt advises determining the patient's metabolic rate,

and testing him for undulant fever and tularemia before establishing the diagnosis of cardiac neurasthenia.

In treating the patient, it seems preferable for the physician to avoid using a psychiatric concept as the basis for the cardiac neurosis. As a matter of fact, the psychoneurosis may be created by such emphasis, and it is far better to approach the problem by stressing the low incidence of true abnormalities in cardiac function rather than urging the patient to be too careful and cautious.

One should explain considerately to the patient that his heart is not impaired and tell him why it seems to beat too fast. The physician should also explain any murmurs which may be present, if there is no other sign of failure or impending failure, and to tell him what effect a continuation of his fears will have on his future well being.

A. E.

GENERAL PRACTICE RESIDENCY

THE American Medical Association has announced approval of a residency specifically designed to train physicians for general practice. Previously the A.M.A. Council on Medical Education and Hospitals had approved hospitals for general or mixed residencies, which were rather loosely organized, to provide additional experience following internship.

The residency for general practice will provide supervised training in the four major clinical divisions—internal medicine, surgery, obstetrics-gynecology, and pediatrics—as well as in the auxiliary services of anesthesiology, pathology, and radiology.

Some 870 hospitals which the Council had previously accredited for general residency training will be expected to reorganize their programs in accordance with the new requirements for the general practice residency.

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Consultation Service

This special consultation information service is offered as a regular monthly feature of *Postgraduate Medicine*. Readers are invited to call on this Service for answers to difficult medical problems from members of our Editorial Board best qualified to help. Each question will be answered by mail and those of general interest will be published each month. Address all communications to Consultation Service, *Postgraduate Medicine*, 516 Essex Building, Minneapolis 3, Minnesota.

STILBESTROL FOR CHRONIC MISCARRIAGE

QUESTION: Could you please give me the reason for the use of stilbestrol in the prevention of chronic miscarriage and also, the dosage recommended?

Also, could I have some data on the use of stilbestrol in the prevention of toxemia of pregnancy and the dosage schedule?

M.D.—New York

ANSWER: No one reason can be given in reply to the question because the use of diethyl-stilbestrol in abortions, threatened or habitual, and in prevention of toxemia of pregnancy, is based on an exceedingly complicated, and therefore doubtful, chain of theoretically interlocking endocrinologic reactions.

Briefly, the most important points of these are postulated as follows:

(a) There is a toxin in the circulating blood of women during menstruation, late pregnancy toxemia, and labor.

(b) This toxin develops and appears in the blood stream as the result of failure of certain hormonal support from endometrium and decidua.

(c) There is a lag in time between withdrawal or failure of the hormone support and the occurrence of symptoms.

(d) Certain endocrine dysfunction, namely abnormally high concentration of serum chorionic gonadotrophin is possibly not being used for its normal stimulation of estrogen and progesterone, so that

(e) Administration of estrogenic substance is necessary to make both a direct supply and a stimulation of autogenous estrogen production necessary for maintenance of pregnancy.

Neither the correctness of the views of the originators (O. W. Smith and G. V. S. Smith) of this therapy, nor the broad scope of its therapeutic value have yet been established. The concept was based on theory, the development of the therapy on animal experimentation, and the clinical application to patients is on trial. Endocrinology is still an inexact and uncertain branch of science, with many phases highly theoretical.

The standing of the Smiths has warranted reception of their recommendations. Clinicians may not understand or be able to follow their exact reasoning or judge the accuracy of the theoretic underlying views. Nevertheless, enough is known to justify our accepting the Smiths' recommendation, if we can be sure that large doses of stilbestrol are not harmful to pregnant women as they are in some respects to nonpregnant women. In instances of threatened or repeated abortion, for example, a clinical trial may be undertaken and enough clinical trials will presently settle the question.

In the meantime, we are using the method because workers of authority and repute have said there are valid reasons, and like that of certain other treatments, we fear we may be failing to use something which might be of value.

I believe, though am not yet prepared to express an opinion, that favorable results have been obtained in our clinic in the treatment of threatened abortion. Certainly, the results have been more encouraging than with the use of progesterone. In the use of stilbestrol for habitual abortion, I have not yet been willing to abandon the simultaneous use of thyroid substance or of iodides to stimulate the patient's thyroid.

I am extremely critical of such "clinical investigations" as one recently reported where an attempt was made by deliberate overdosage without indications solely to determine how much stilbestrol pregnant patients could tolerate without harm. Apparently the possible ill effects on the mothers or fetuses did not deter this investigator, and we know that there are certain decidedly ill effects in nonpregnant women.

Answering the second part of the question, the theory of the use of stilbestrol in toxemia of pregnancy is approximately the same as that for prevention of abortion. It is said also to be of value in diabetes complicating pregnancy, and that it is a preventive against premature labor.

It should not be given, we are told, in the early weeks of pregnancy when the placenta is forming; it should be discontinued after the thirty-fifth week.

Stilbestrol can be used to stop lactation, but given during the pregnancy (not later than the thirty-fifth week) it does not interfere with the development of lactation.

It is indeed a versatile therapeutic measure, if all this proves correct.

The dosages recommended are (after the seventh week) 5 mg. daily, this daily dose to be increased by 5 mg. every second week until near the middle of pregnancy when it may be thus increased every week.

If the medication is not begun until later in the pregnancy (after the middle thereof) one is advised to begin with 30 mg. per day increasing weekly as above. I have not yet used such high dosage as this latter, but have followed directions for treatment of threatened or habitual abortions.

PAUL TITUS

PARKINSON'S DISEASE

QUESTION: What are the indications for operation of division of the pyramidal tracts in the spinal cord in the treatment of Parkinson's disease? Is it a recommended procedure?

M.D.—Illinois

ANSWER: Among the various operations for the relief of Parkinson's disease has been the division of the pyramidal tracts in the spinal cord. It has been given a clinical trial in the hands of a number of investigators and has not proved successful as a means of controlling the disabling tremor. It is not a recommended procedure.

SENSITIVITY TO STREPTOMYCIN

QUESTION: Do patients develop a sensitivity to streptomycin? How does it manifest itself?

M.D.—Pennsylvania

ANSWER: Yes—and the sensitivity manifests itself as a contact dermatitis. It is found among nurses, technicians and pharmacists, and other individuals who handle the material repeatedly. Many cases are reported in the literature. The last report by S. W. Simon (J. Allergy 20:56-61 [January] 1949) is very comprehensive and covers the subject completely.

HARRY L. ROGERS

ABSORPTION OF PENICILLIN

QUESTION: What precautions must be taken to insure best absorption of penicillin by mouth?

M.D.—Ohio

ANSWER: Penicillin by mouth is best given in the form of 50 million unit tablets of crystalline penicillin G. The most important factor involved in insuring that an adequate amount of penicillin is absorbed is dosage. Under most circumstances the initial dose should be 200,000 to 300,000 units; subsequent doses, 100,000 units every two to four hours. The actual dosage required in an individual case will depend upon the nature and severity of the infection. No other precautions are necessary.

FRANCIS G. BLAKE

CHRONIC MYELOID LEUKEMIA

QUESTION: In the treatment of chronic myeloid leukemia in a woman of 40, can urethane be used in conjunction with Fowler's solution, both to be given orally?

M.D.—Florida

ANSWER: It is our opinion that both urethane and Fowler's solution can be used to advantage in the control of chronic myeloid leukemia. Since either alone may be efficacious, there seems to be no reason to give two toxic substances simultaneously as there has been no demonstration of a synergistic effect.

Of the two substances, urethane is the least toxic and probably the most effective over a period of months.

Dosage for urethane: 1 gm. daily for two days, 2 gm. for two to three days, then 3 to 5 gm.; should be discontinued when the blood count goes below 15,000. It must be remembered that this material is excreted very slowly and its influence may be present over many weeks after the discontinuance of the drug. If possible it should be given intermittently and not continuously, although it has been given continuously for more than one year.

R. LEE CLARK, JR.

NEUROCIRCULATORY ASTHENIA AND GRAVES' DISEASE

QUESTION: What are the signs in the differential diagnosis of neurocirculatory asthenia and Graves' disease?

M.D.—California

ANSWER: The most helpful sign to differentiate Graves' disease from neurocirculatory asthenia is the temperature of the hands. In neurocirculatory asthenia the hands are almost invariably cold and moist and in Graves' disease they are almost invariably warm and moist.

Persistence of tachycardia at rest, absence of marked sinus arrhythmia or slowing of the pulse with deep respiration, persistent elevation of the basal metabolic rate, lowered blood cholesterol, response to a therapeutic trial on one of the antithyroid drugs, eye signs, and loss of weight, all afford objective evidence of the presence of Graves' disease, as does the presence of a solid goiter.

Absence of these objective signs of Graves' disease suggests that neurocirculatory asthenia is the cause of the difficulty. When in doubt, a trial on propyl thiouracil is far preferable to performing a thyroidectomy.

GEORGE CRILE, JR.

DIABETIC ACIDOSIS

QUESTION: Should glucose, as well as insulin, be given in the early stages of the treatment of diabetic acidosis while the blood sugar is still high?

M.D.—Kansas

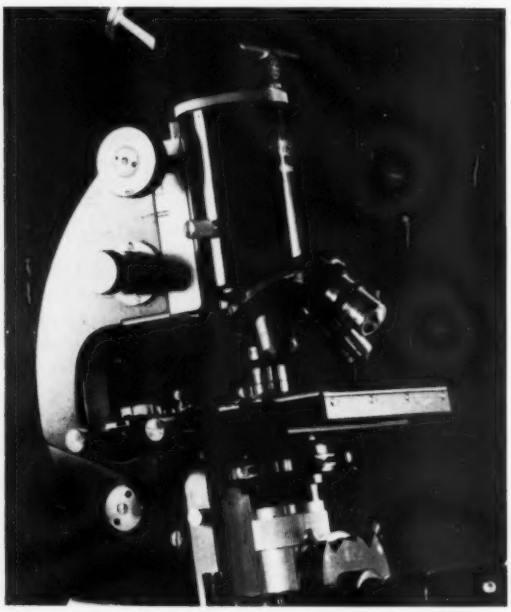
ANSWER: There are two schools of thought regarding this procedure. The conservative people who have treated large numbers of patients with diabetic acidosis and coma, from the mild to the very severe degrees, do not give glucose in the early stages of acidosis when the blood sugar is very high, but they do give large doses of insulin.

The dosage of insulin depends, of course, upon the degree of acidosis, the height of the blood sugar, the age of the patient, and the length of time he or she has had diabetes. When the blood sugar begins to fall, or when the patient begins to be conscious, we give glucose by mouth, when possible; if not, small doses intravenously when necessary.

JAMES E. PAULLIN

New Drugs and Instruments

Information published in this department has been supplied by the manufacturers of the products described.



NEW PHASE-CONTRAST MICROSCOPE

DESCRIPTION: Features of the instrument are (1) an auxiliary lens built in the microscope tube, replacing ordinary telescope attachment used for centering the phase ring; (2) a pancratic substage which provides for an annular source of variable diameter to match any phase-ring and any condition illumination; (3) a built-in source of light for visual observation.

PRODUCER: The Galileo Corporation of America, New York, N. Y.

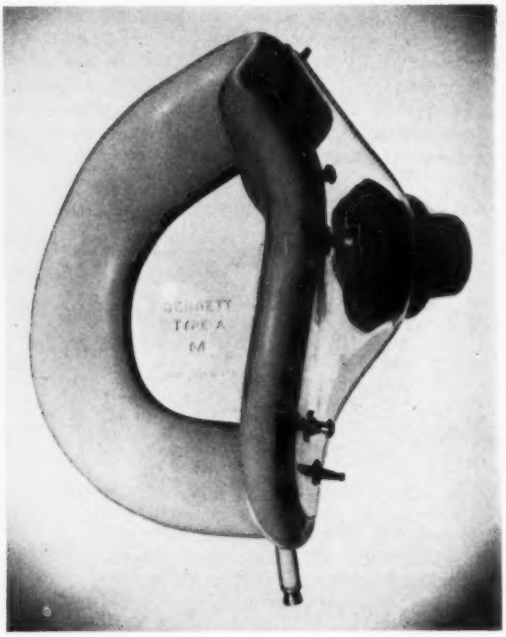
SEVINON

PURPOSE: Treatment of psoriasis.

COMPOSITION: Purified oral undecylenic acid in capsule form. This product is an eleven carbon straight-chain unsaturated fatty acid, closely related to oleic acid.

INDICATIONS FOR USE: Preliminary reports on the use of Sevinon in psoriasis and dermatitis indicate that new encouragement may be offered to these patients, although no final claims for the therapeutic efficacy of undecylenic acid in these intractable conditions can be made at this time. Consequently, Sevinon capsules have been made available for further study and clinical evaluation.

PRODUCER: Schering Corporation, Bloomfield and Union, N. J.



BENNETT "TIGHT SEAL" MASK

DESCRIPTION: Consists of a lightweight, low dead air space, plastic face piece. The face cushion is made of soft rubber with a sponge rubber center. Worn bladders can be replaced. Fittings for all leading makes of anesthesia, metabolism, and oxygen equipment are available.

PRODUCER: Oxygen Therapy Sales Co., Los Angeles 27, Calif.

ORTHOXINE* HYDROCHLORIDE, ABERGIC* TABLETS

PURPOSE: Bronchodilator and smooth muscle inhibitor.

COMPOSITION: Beta-(ortho-methoxyphenyl)-isopropyl-methylamine hydrochloride. Each compressed tablet contains 100 mg. Orthoxine hydrochloride.

INDICATIONS FOR USE: Relieving symptoms of allergic rhinitis, acute urticaria, and gastrointestinal allergy as well as bronchial asthma.

DOSAGE AND ADMINISTRATION: For controlling asthmatic attacks, urticaria, and allergic rhinitis, the usual dose is 50 to 100 mg. repeated if necessary every three to four hours. Children, 25 to 50 mg.

HOW SUPPLIED: Bottles of 100 and 500 tablets.

PRODUCER: The Upjohn Company, Kalamazoo, Mich.

*Trademarks.

NEW RUOY PHOTROMETER

DESCRIPTION: Ruoy Photrometer is precalibrated for 38 common clinical tests. Supplied with every unit is a handbook containing calibration tables for each clinical method.

The optical system consists of a lamp, precision ground mirror, filters, and absorption cell. Light traversing this system falls upon a barrier layer photoelectric cell, generating a current which actuates a direct reading microammeter.

Of twelve filter spaces provided, ten contain narrow spectral band filters which cover the entire visible spectrum. Two other spaces allow for special work.

PRODUCER: E. Leitz, Inc., New York 13, N.Y.

DIPHENTOIN

PURPOSE: Treatment of epilepsy.

COMPOSITION: Each capsule contains diphenylhydrantoin sodium, 1½ gr. (0.1 gm.).

DOSAGE AND ADMINISTRATION: Adults, 1½ gr. three times daily, increased as necessary. Average adult dosage range is from 4½ to 9 gr. per day. Older children, 1½ gr. daily. Accompany each dose with a half glass of water.

HOW SUPPLIED: Blue-top capsules, bottles of 100 and 1,000.

PRODUCER: The S. E. Massengill Co., Bristol, Tenn.

ALRAC and ALRACOMP

PURPOSE: Treatment of hyperacidity and peptic ulcer.

COMPOSITION: Each Alrac tablet contains:

Dihydroxy aluminum aminoacetate	0.333 gm. (approx. 5 gr.)
Magnesium trisilicate	0.167 gm. (approx. 2½ gr.)

Each Alracomp tablet contains:

Dihydroxy aluminum aminoacetate	0.333 gm. (approx. 5 gr.)
Magnesium trisilicate	0.167 gm. (approx. 2½ gr.)
Homatropine methylbromide	0.864 mg. (approx. 1/75 gr.)
Phenobarbital	16 mg. (approx. ¼ gr.)

CAUTION: To be dispensed only by or on the prescription of a physician. Warning: Phenobarbital may be habit forming.

DOSAGE AND ADMINISTRATION: Alrac: 1, 2 or more tablets between meals and on retiring, or as prescribed by physician. Tablets may be chewed or swallowed whole. Alracomp: May be prescribed between meals, alone or in conjunction with Alrac, depending on the degree of sedation required.

HOW SUPPLIED: Packages of 100 tablets.

PRODUCER: Reed & Carnick, Jersey City, N. J.

BI-PEN

PURPOSE: Dual penicillin preparation.

COMPOSITION: Each dose consists of 300,000 units of crystalline procaine penicillin G and 100,000 units of buffered crystalline penicillin G potassium.

DESCRIPTION: Upon intramuscular injection the crystalline potassium penicillin is promptly absorbed leading to initial plasma penicillin levels which may be as high as 4.0 units per cc. Prolonged absorption of the procaine penicillin maintains levels above average requirements for twenty-four hours in virtually all patients.

HOW SUPPLIED: As a dry powder which is stable in the original vial for eighteen months at room temperature. Available in a combination package containing a single dose (400,000 units) together with a 1 cc. size ampule of sterile distilled water, in boxes of 5 single dose vials, and in a multiple dose vial containing 2,000,000 units.

PRODUCER: C. S. C. Pharmaceuticals, division of Commercial Solvents Corporation, Terre Haute, Ind.

LIQUAEMIN (High Potency)

PURPOSE: Heparin preparation.

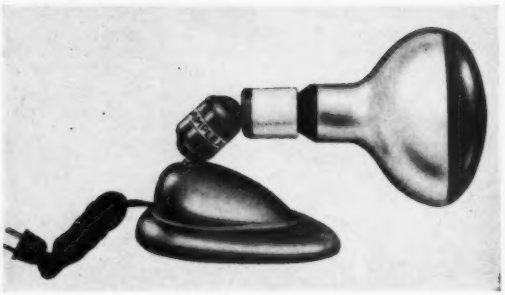
COMPOSITION: Liquaemin (High Potency) contains 50 mg. of heparin sodium per cc. of solution.

INDICATIONS FOR USE: Certain thrombo-embolic complications, particularly those which occur during coronary thrombosis, acute myocardial infarction, phlebothrombosis, and thrombophlebitis, as well as in all other disturbances in which anticoagulant therapy has been shown to be of value.

DOSAGE AND ADMINISTRATION: By the intermittent injection method—intravenous, subcutaneous, or intramuscular injections—dosage ranges from 25 to 100 mg. given at intervals of three to twelve hours, depending on patient's response as determined by the clotting time. Coagulation time should be maintained at twenty to thirty minutes by the Lee-White method or about fifteen minutes by the capillary tube method.

HOW SUPPLIED: In 10-cc. vials, each vial containing a total of 500 mg. of heparin sodium. Liquaemin is still available in its original strength of 10 mg. of heparin sodium per cc.

PRODUCER: Organon, Inc., Orange, N. J.



HOUSEHOLD HEAT LAMP

DESCRIPTION: Made of Corning ruby-red glass and inside lined with silver reflecting surface, the lamp fits any AC-DC household socket. It is provided with a lamp holder designed with a Swivelite heatproof porcelain socket.

PRODUCER: Amplex Corporation, Brooklyn, N. Y.

ABBOTT DECILITERS

DESCRIPTION: Each container is of 100 cc. capacity with Goldy seal. Designed to reduce waste involved in partial use of larger containers, and eliminate danger of contamination and reactions sometimes encountered when repeated infusions are made from a single large container.

Five solutions for pediatric use are now available in Abbott Deciliters: ISOTONIC SODIUM CHLORIDE, U. S. P.; DEXTROSE, U. S. P. 2½% W/V IN HYPOTONIC SODIUM CHLORIDE SOLUTION; LACTATED RINGER'S SOLUTION, U. S. P.; DEXTROSE, U. S. P. 2½% W/V IN LACTATED RINGER'S SOLUTION, and SODIUM L-LACTATE, 1/6 MOLAR.

DOSAGE AND ADMINISTRATION: To administer, remove safety seal and bottle cap. Draw fluid into large sterile syringe and inject intravenously or subcutaneously. Discard unused fluid, as Deciliters contain no bacteriostatic agent.

PRODUCER: Abbott Laboratories, North Chicago, Ill.

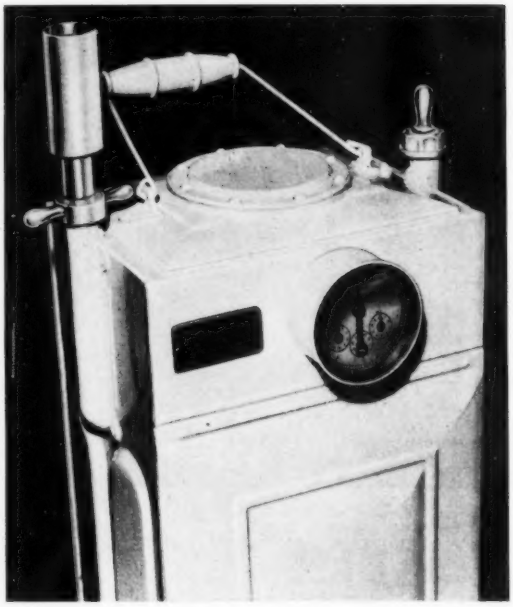
NEW STONE-JARDON IMPLANT

DESCRIPTION: Permits greater motility and reduces operating time. The slanting flange creates a deeper lateral fornix, allowing greater motility to the eye portion. The implant itself can turn further laterally as the new design incorporates a bulge which acts as a fulcrum when the lateral rectus muscle is sutured over this portion of the implant.

Provides space beneath the tantalum mesh so suture needles can be passed through eliminating necessity for tunneling the mesh.

A neck below the flange forms a groove for the conjunctiva. With a purse string suture, the conjunctiva can be drawn into the groove rather than suturing directly to the mesh.

PRODUCER: American Optical Company, Southbridge, Mass.



RESPIRATORY METER

PURPOSE: For respiratory tests and the evaluation of patients who are candidates for chest operations.

DESCRIPTION: This modified portable test meter, AS8-5/150, is equipped with synthetic molded diaphragms, hand hole cover, handle liter dial, and a special hose nozzle on the inlet for connecting to a suitable high velocity valve by means of rubber tubing. The large dial pointer makes one revolution per liter, and the index reads from 0.01 to 1000 liters.

PRODUCER: American Meter Company, New York, N. Y.

PYRIBENZAMINE NASAL SOLUTION IN NEBULIZER

PURPOSE: Antihistaminic for relief of nasal allergy.

COMPOSITION: Solution contains 0.5 per cent of the active antihistaminic agent in an isotonic aqueous solution buffered at *p*H 6.2. The pocket-size nebulizer contains several hundred applications of the solution. The tube is only partially filled, leaving sufficient air to create a spray.

INDICATIONS FOR USE: In hay fever and vasomotor rhinitis.

DOSAGE AND ADMINISTRATION: One application to each nostril every three or four hours is recommended. Less frequent application often suffices.

HOW SUPPLIED: Nebulizers containing 7.5 cc. of Pyribenzamine Nasal Solution each.

PRODUCER: Ciba Pharmaceutical Products, Inc., Summit, N. J.

Leaves from a Doctor's Diary

By Maurice Chideckel

June 1 . . . Men move and develop under stress of events. They become modified by the pressure which works on all flesh. Growth and change, progress and success, regression, frustrations, and defeats are the ways of the world. So are love and hate. There are men with the anxiety to please and make someone happy, and there are those with streaks of sadism, a morbid lust for hurting for which they can evolve no valid explanation, just as the depressive psychotic can give no reason for the desire to perish.

It is all hidden in the mystery chamber we call mind, mind, balanced or distorted. This perhaps may account for the psychogenic causes of so many diseases, and why *psychosomatic* became the glib vocabulary of our profession. I am beginning to believe, as many others do, that peptic ulcer, hypertension, certain forms of asthma, and even severe cardiac distress are the results of psychic conditions, of conflicting emotional factors. Sufficient concrete information has accumulated to substantiate this theory.

Here is Pauline Bentley whose relentlessly austere husband, a school teacher, knows no humor, and was never known to smile. In a playful mood she asked her husband: "Darling, will you love me when I'll be old and ugly?" He replied seriously: "Am I not doing it now?" Tears, screams, and then hysterical convulsion. "So I am already old and ugly," were the mutterings between seizures. "Go and tell her that you did not mean it," I ordered him. Solemnly he protested: "But I did mean it. Are you endeavoring to make a liar out of me?"

There is the exuberantly learned and ebulliently humorous Professor Patrick Reynal, whose lectures are listened to with appraising ears by many scholars. Between lectures, he amuses his classes with humorous tales. He no longer laughs, not for the present.

Two masked bandits entered the exclusive restaurant where he sat and ate. One bandit stood near the door, probably watching for the approach of police. The other, with guns in hand, said gently: "Ladies and gentlemen, any one in favor of leaving this place alive should raise his or her hands, and keep them raised."

When the soft speaking thug approached the professor the learned gentleman said laughingly: "You are evidently a president of a lodge." At the sound of the voice, the one standing near the door with face to the street ran out, and was followed by his pal. Late at night, Dr. Reynal entered the room of his son, a student of philosophy, to relate his experiences. The son was not in. But half a dozen watches of which the guests were robbed, and his wallet without money were on the table. At the moment of this writing, the professor is in oxygen due to dyspnea and cyanosis, and the shock may kill him.

What about Dennis Crawford, a sentimentalist, extravagantly tender to others, much more than to himself. His life savings consisted of one thousand dollars, which he gave to a friend to invest. The friend died suddenly. I was summoned to the funeral parlor, where Crawford became combative and threatened to tear the corpse limb from limb if he does not return his money. The gentlemanly, well-mannered man was without inhibition as to vocabulary. The dead man was called every name Webster ever knew. He finally regained his composure and is now in bed with a bleeding peptic ulcer.

• • •

June 2 . . . Events of one morning.

Psychologist Horn lectured on boredom and said that boredom is a rebellion against monotony, a reaction to sameness which leads to a desire for an escape. His boring talk, the monotony of his voice, and the exit of most of his listeners proved his opinion right.

Old Lozinsku came to the clinic and offered five hundred dollars to any one who will convert his myopia into farsightedness. He was told that the beautiful young woman living across the street from him, who never pulls down her blinds, walks around for hours in a transparent gown, and he can't see her.

Foster Kuffer is a gentleman, every inch of him, with the exception of the few inches from the neck up. Kuffer, by the way, is a man of considerable means. His son was admitted with Hodgkin's disease under my care. Administration of nitrogen mustard wrought wonders. In my office sat the father and talked. "Pay you and pay the hospital? Preposterous. Look at the business that it'll bring you when the papers begin to print news about his recovery. You should pay me. You may pay my son. It's all right with me. All right, all right. I'll tell you what. I'll pay for the mustard. Satisfied?"

Events in the evening:

Headache and insomnia. Told the elderly patient not to take his troubles to bed. "Must," he said. "The old lady wouldn't sleep by herself."

Came to inform Mrs. Middler that the sudden greying of the hair of her 13-year-old son may be a sign of degenerative process and I want him under observation. But who could talk to an infuriated woman? She saw the milkman kiss her maid, a strikingly pretty little thing. "From now on," screamed the lady of the house, "I, understand, I will take in the milk." The maid smiled. "It won't do you any good, Mrs. Middler. He'll never kiss *you*."

* * *

June 8 . . . I was invited to a chicken dinner. Near me sat Dr. Field Stevens, who never stops talking shop. As the guests sat around the table, all lay people, Stevens opened up: "You know what? Dicumarol has no effect on the EKG. And you want to know something else? Estimation of blood cholesterol is of little value. . ."

The lady of the house, a dignified elderly woman, began to make a racket with the knives and forks. "So much noise," the doctor protested, "I can't hear myself talk."

"That's why I am making that noise," she admitted. "We'll lose nothing and neither will you. Now, doctor, be a sport. Carve the chicken."

The result of his carving was disastrous. "The way you cut the chicken, I would not let you operate on me," she said smilingly.

"Well," spoke the doctor, "you shouldn't be afraid. You are no longer a chicken. Just an old hen." He thought it was funny. That's why he laughed. The hostess thought otherwise. He received a letter in the morning to sever his relations with the family, that he is no longer wanted as a family doctor. He meditated philosophically: "The man who always lies is a bad man. The one who always tells the truth is worse. So it seems to me."

* * *

June 10 . . . Passing by Alpert's Clothing Store, I stopped to inform him that his child is considerably improved. The 8-year-old boy with tuberculous meningitis was progressing well while being given streptomycin intrathecally.

I like Adolph Alpert for his dispassionate, placid reasonableness in all his dealings. He was happy at the news I just imparted.

A "gentleman of the road," the typical bum one sees on the screen, unshaved, raggedy and odorous, entered the store. "How much for this pair of pants?" he asked. He was told the price is five dollars. "Ain't got five dollars." How much has he got? "Ain't got nothin'." "Well," said Mr. Alpert, "I'll be charitable today and let you have the pants for nothing." "In that case," said Mr. Bum, "I'll take two pairs."

* * *

June 13 . . . Mrs. Boyd came to inform me that the medicine I gave her (rutin and ascorbic acid) cured her completely. She has been suffering from essential hematuria for a long time. In the consultation room was her husband, unbeknown to her, receiving intramuscular injection of penicillin for a freshly contracted case of gonorrhea. Mrs. Boyd sat in the waiting room and talked to another woman whom she met for the first time.

Said Mrs. Boyd: "My husband, the best on earth. He is now better than ever. He'd kill himself for me." Said the other woman: "Listen to me. When a husband becomes too good, watch him. There is always another woman behind his goodness."

I managed to let our Mr. Boyd out through the back door, then called in the woman. A Mrs. Garrington. She too received penicillin for the same ailment. "I don't know," she spoke, "who gave it to who; I to him (Boyd) or he to me. What, that woman is his wife? Hmm. So I gave her good advice."

Then came Mrs. Boyd. "No more bloody urine," she said happily. "But—well, I have some pain, and a discharge. You know, doctor, if I didn't know my husband as I do, well, I'd suspect.

* * *

June 15 . . . Before a lay group of young women, Dr. Mildred Hudson gave the weekly talk on "Know Thyself" series. This time it was a lecture on abnormal vaginal bleeding. After mentioning growths, the common cold, infectious diseases, avitaminosis, traumatic lesions, endometriosis, she dwelt at length on the emotional basis, say, the fear of coitus.

"What's a coitus?" one girl loudly asked the woman next to her. She answered just as loud. "Physical union, you know." Again: "What's that?" This time the explanation was whispered in her ear. A loud and hysterical laughter. "Afraid of that? Nuts!"

That laughing girl was in my office the next day with plantar warts. As I was paring down the corneous upper layer so I could paint the wart with collodion, and then apply podophyllin, she talked: "Did you hear the latest? Some girls are afraid of—." She used an unprintable term. Suddenly she turned philosopher. "I tell you, marriage is no lottery. I was married twice. In a lottery you win sometimes. In marriage, never."

* * *

June 18 . . . Two young boys, 17 and 18, both making frenzied efforts to pass examinations. Both living in one room. Three weeks ago the younger was committed to a mental hospital, being a pronounced schizophrenic. Today the other proved a definite case of de-

(Continued on page 50)